EXHIBIT 1

[redacted]

CONTAINS INFORMATION DESIGNATED HIGHLY CONFIDENTIAL BY SAREPTA

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (GBW)
SAREPTA THERAPEUTICS, INC., Defendant and Counter-Plaintiff v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff and Counter-Defendants.	

NIPPON SHINYAKU CO. LTD.'S AMENDED FINAL INFRINGEMENT CONTENTIONS

Pursuant to Paragraph 7(c) of the of the Proposed Scheduling Order (D.I. 100-1), Plaintiff Nippon Shinyaku Co. Ltd. ("Nippon Shinyaku") provides the following **amended** final infringement contentions, including claim charts relating each known accused product to the asserted claims each such product allegedly infringes, to Defendant/Counter-Plaintiff Sarepta Therapeutics, Inc. ("Sarepta").

Nippon Shinyaku provides this disclosure based on the information and evidence available to it at this time, without the benefit of full discovery. Nippon Shinyaku notes that ~~the Court has yet to issue its claim construction order relating to certain asserted patents, and that~~ fact discovery remains ongoing in this case. Nippon Shinyaku therefore reserves its right to make any modifications, additions, deletions, or supplementations to this disclosure as

additional evidence and information become available, or as is otherwise appropriate and permissible.

I. IDENTIFICATION OF ASSERTED PATENTS AND CLAIMS

Based on Nippon Shinyaku's investigation to date, Sarepta, either alone or in conjunction with others, has infringed, and continues to infringe, the following claims:

- U.S. Patent No. 9,708,361 ("the '361 Patent," D.I. 2-2): Claims 1 and 3-7;
- U.S. Patent No. 10,385,092 ("the '092 Patent," D.I. 2-3): Claims 1-3;
- U.S. Patent No. 10,407,461 ("the '461 Patent," D.I. 2-4): Claims 1-2;
- U.S. Patent No. 10,487,106 ("the '106 Patent," D.I. 2-5): Claims 1-2;
- U.S. Patent No. 10,647,741 ("the '741 Patent," D.I. 2-6): Claims 1-12;
- U.S. Patent No. 10,662,217 ("the '217 Patent," D.I. 2-7): Claims 1-4; and
- U.S. Patent No. 10,683,322 ("the '322 Patent," D.I. 2-8): Claims 1-10.

Collectively, the above identified patents shall be referred to herein as the "NS Asserted Patents," and the above identified claims shall be referred to as the "NS Asserted Claims."

The NS Asserted Claims can be divided into three specific types. The first type of claim, which makes up the majority of the NS Asserted Claims, is directed to a specific product, namely oligomers or subclasses thereof. These claims shall be referred to herein as the "NS Product Claims" and include:

- '361 Patent: Claims 1 and 3-7;
- '092 Patent: Claims 1-3;
- '461 Patent: Claims 1-2; and
- '106 Patent: Claims 1-2.

The second type of claim is directed toward a method of using a specific product. These claims shall be referred to herein as the "NS Method of Use Claims" and include:

- '741 Patent: Claims 1-12; and
- '217 Patent: Claims 1-4.

The third type of claim is directed toward a method of making a specific product. These claims shall be referred to herein as the "NS Method of Making Claims" and include:

- '322 Patent: Claims 1-10.

Nippon Shinyaku reserves the right to supplement or amend this identification of the NS Asserted Claims as discovery in this case proceeds.

II. INFRINGEMENT CONTENTIONS

Based on Nippon Shinyaku's investigation to date, Nippon Shinyaku identifies Sarepta's product, VYONDYS 53 (golodirsen) as the accused product (e.g., with respect to the NS Product Claims), the manufacturing process for VYONDYS 53 (golodirsen) as the accused manufacturing method (e.g., with respect to the NS Method of Making Claims), and use according to the prescribing information of VYONDYS 53 (golodirsen) and/or Sarepta's marketing literature regarding administration of VYONDYS 53 (golodirsen) as the accused treatment method (e.g., with respect to the NS Method of Use Claims). Sarepta has made, sold, offered for sale, used, and/or imported into the United States VYONDYS 53 (golodirsen) such that it infringes, either literally or under the doctrine of equivalents, the NS Asserted Claims under at least 35 U.S.C. § 271(a), (b), (c) and/or (g), as set forth in detail below and in the attached Appendices A1-A7.

Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

A. Infringement of the NS Product Claims

As set forth in Appendices A1-A4, VYONDYS 53 (golodirsen) meets each of the limitations of the NS Product Claims either literally or under the doctrine of equivalents. NS only asserts infringement of the '361 Patent under the doctrine of equivalents. For the reasons described below, Sarepta directly and/or indirectly infringes each of the NS Product Claims under at least 35 U.S.C. § 271(a), (b), and (c).

1. Sarepta Directly Infringes the NS Product Claims Under 35 U.S.C. § 271(a)

Sarepta directly infringes and will continue to directly infringe the NS Product Claims under 35 U.S.C. § 271(a) by importing, offering for sale and/or selling VYONDYS 53 (golodirsen). Sarepta's offers for sale and/or sale of VYONDYS 53 (golodirsen) is shown at least by certain sales data produced by Sarepta. *See e.g.,* SRPT-VYDS-0006844–6978; SRPT-VYDS-0007097–7262. Nippon Shinyaku may rely upon any and all sales data produced by Sarepta in this case, including Sarepta's [redacted] Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted] Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of sales and/or offers for sale, particularly in light of Sarepta's Response to Interrogatory No. 3, in

which Sarepta has indicated that information, including sales and/or importation information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15 (dated April 11, 2022).

Sarepta also directly infringes and will continue to directly infringe the NS Product Claims under 35 U.S.C. § 271(a) by making VYONDYS 53 (golodirsen). Specifically, Sarepta informed that FDA that:

[redacted]

SRPT-VYDS-0006997 at -98. To the extent that Sarepta argues that it does not directly manufacture golodirsen, but contracts out the manufacture of golodirsen to another entity (e.g., [redacted]), Sarepta directs and controls the manufacture of golodirsen such that the performance of every step manufacturing step is attributable to Sarepta. *Id.*; *see also BMC Res., Inc. v. Paymentech, L.P.*, 498 F.3d 1373, 1379-81 (Fed. Cir. 2007); *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318 (Fed. Cir. 2008). Indeed, the prescribing information for VYONDYS 53 (golodirsen) states that it is:

Manufactured for:
Sarepta Therapeutics, Inc.
Cambridge, MA 02142 USA

Highlights of Prescribing Information (Dec. 12, 2019) § 17 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 17. And Sarepta affirmatively holds itself out as "[redacted]

[redacted] Nippon Shinyaku may further rely upon evidence relating to Sarepta's arrangements with third parties relating to the making of VYONDYS 53 (golodirsen), such as its arrangements with [redacted] Accordingly, Sarepta directly infringes and will continue to directly infringe the NS Product Claims under 35 U.S.C. § 271(a) by making VYONDYS 53 (golodirsen). Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's manufacturing, particularly in light of Sarepta's Response to Interrogatory No. 3, in which Sarepta has indicated that information, including manufacturing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15 (dated April 11, 2022).

Sarepta also directly infringes and will continue to directly infringe the NS Product Claims under 35 U.S.C. § 271(a) by using VYONDYS 53 (golodirsen). Specifically, Sarepta has used VYONDYS 53 (golodirsen) in testing, including pre-clinical and clinical testing. *See e.g.,* Highlights of Prescribing Information (Dec. 12, 2019) § 12-14 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12-14. To the extent that Sarepta argues that it does not directly test golodirsen, but contracts out the testing of

golodirsen to another entity, Sarepta directs and controls the testing of golodirsen such that the performance of the testing is attributable to Sarepta. *Id.* Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's testing, particularly in light of Sarepta's Response to Interrogatory No. 10, in which Sarepta has indicated that information, including testing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 21-22 (dated April 11, 2022).

2. Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.**Sarepta Indirectly Infringes the NS Product Claims Under 35 U.S.C. §§ 271(b) and 271(c)**

Indirect infringement under both 35 U.S.C. § 271(b) and (c) requires knowledge of the NS Asserted Patents and knowledge of infringement. Both types of indirect infringement also require a third-party direct infringer. Induced infringement under 35 U.S.C. § 271(b) requires that that Sarepta also induce or encourage another party to directly infringe. Contributory infringement under 35 U.S.C. § 271(c) also requires that that Sarepta offer to sell, sell, or import a component that is a material part of an invention that is especially made or adapted for use in infringement, and does not have substantial noninfringing uses. As set forth below, Sarepta induces and contributes to infringement under both 35 U.S.C. § 271(b) and (c).

a. Sarepta Had Knowledge of the NS Asserted Patents

Sarepta had knowledge of each of the NS Asserted Patents at least as of each of their

issuance dates and/or [redacted]. Below is certain bibliographic information found on the face of each of the NS Asserted Patents:

Patent	Issue Date	Filing Date of Application	Earliest Priority Claim
'361 Patent	July 18, 2017	Feb. 6, 2015	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011
'092 Patent	Aug. 20, 2019	Mar. 20, 2019	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011
'461 Patent	Sep. 10, 2019	Mar. 26, 2019	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011
'106 Patent	Nov. 26, 2019	Mar. 29, 2019	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011
'741 Patent	May 12, 2020	June 24, 2019	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011
'217 Patent	May 26, 2020	Dec. 12, 2019	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011
'322 Patent	June 16, 2020	Dec. 17, 2019	App. No. 13/819,520, which was filed as PCT/JP2011/070318 on Aug. 31, 2011

As shown by the bibliographic data, each of the NS Asserted Patents is included in the same patent family, stemming from a PCT application filed on August 31, 2011. The US

application (No. 13/819,520) of the PCT filing was published as US 2013/0211062 A1 on August 15, 2013.

Sarepta has "exclusive rights to [U.S. Patent Nos. 9,994,851 ("the '851 Patent"); 10,227,590 ("the '590 Patent"); and 10,266,827 ("the '827 Patent") (collectively, "the UWA Patents")] for the treatment of muscular dystrophies and the right to enforce [the UWA Patents]." D.I. 89 Counterclaims at ¶¶ 21-23. [redacted] Each of the UWA Patents, including the '851 Patent, identifies on its face the publication no. US 2013/0211062 A1, which is a publication in the family of the NS Asserted Patents. Thus, at least as of [redacted] Sarepta knew of the family of the NS Asserted Patents.

Sarepta's activities show that Sarepta tracked this patent family, and gained knowledge of the NS Asserted Patents either at or around [redacted] (for the '361 Patent) or at the time of issuance of the NS Asserted Patents (for the NS Asserted Patents other than the '361 Patent). For instance, in January 2020, Sarepta [redacted] Indeed, Sarepta [redacted]. Later, on June 21, 2021 Sarepta filed seven IPR Petitions with the PTAB seeking to invalidate all of the claims of the NS Asserted Patents. *Id.* at ¶ 66. At this time, Sarepta clearly knew of all of

the NS Asserted Patents, and it would not have challenged the validity of those patents without knowledge that the NS Asserted Patents could be asserted against Sarepta. Finally, on July 13, 2021, Nippon Shinyaku filed this lawsuit and identified its allegations that Sarepta infringes the NS Asserted Patents. D.I. 1. Sarepta was served with the Complaint on July 14, 2021. D.I. 9.

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's knowledge of the NS Asserted Patents and knowledge of infringement, particularly in light of Sarepta's Response to Interrogatory No. 5, in which Sarepta has indicated that information, including information regarding Sarepta's awareness of the NS Asserted Patents will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 17 (dated April 11, 2022).

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's response to Interrogatory No 5 which has not been supplemented to date), as further evidence of Sarepta's knowledge. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding knowledge of the NS Asserted Patents.

b. Sarepta Had Knowledge that VYONDYS 53 Infringes the NS Asserted Patents

As set forth above, Sarepta had knowledge of each of the NS Asserted Patents at least as of each of their issuance dates and/or [redacted]. As of the same time, Sarepta had knowledge that the sale, offer for sale, importation, use, or manufacture of VYONDYS 53 (golodirsen) would infringe the NS Asserted Patents. Specifically, beginning at least around [redacted] (for the '361 Patent) or at the time of issuance of the NS Asserted Patents (for the

NS Asserted Patents other than the '361 Patent), Sarepta began tracking each of the NS Asserted Patents. At this time, Sarepta had already submitted its NDA for VYONDYS 53 (golodirsen). Given the similarities between VYONDYS 53 (golodirsen), or the use or manufacture thereof, and the NS Asserted Claims, Sarepta had knowledge that the sale, offer for sale, importation, use, or manufacture of VYONDYS 53 (golodirsen) would infringe the NS Asserted Patents. This is demonstrated by Sarepta's actions. For instance, [redacted] Later, on June 21, 2021 Sarepta filed seven IPR Petitions with the PTAB seeking to invalidate all of the claims of the NS Asserted Patents. *Id.* at ¶ 66. At this time, Sarepta clearly knew of all of the NS Asserted Patents, and it would not have challenged the validity of those patents without knowledge that the NS Asserted Patents could be asserted against Sarepta. Finally, on July 13, 2021, Nippon Shinyaku filed this lawsuit and identified its allegations that Sarepta infringes the NS Asserted Patents. D.I. 1. Sarepta was served with the Complaint on July 14, 2021. D.I. 9.

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's knowledge of the NS Asserted Patents and knowledge of infringement, particularly in light of Sarepta's Response to Interrogatory No. 5, in which

Sarepta has indicated that information, including information regarding Sarepta's awareness of the NS Asserted Patents will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 17 (dated April 11, 2022).

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's response to Interrogatory No 5 which has not been supplemented to date), as further evidence of Sarepta's knowledge. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding knowledge of the NS Asserted Patents.

c. Third Parties Directly Infringe the NS Product Claims

As described above, Sarepta directs and controls the manufacture of golodirsen such that the performance of every step manufacturing step is attributable to Sarepta. However, to the extent that Sarepta argues that it does not direct or control the manufacture of golodirsen, but contracts out the manufacture of golodirsen to another entity (e.g., [redacted], then the manufacturer of golodirsen (e.g., [redacted] directly infringes the NS Product Claims by making the infringing product (e.g., golodirsen). SRPT-VYDS-0006997 at -98; SRPT-VYDS-0006991 at -92; SRPT-VYDS-0007020 at -22; *see also* SRPT-VYDS-0213330, SRPT-VYDS-0213333, SRPT-VYDS-0213381, SRPT-VYDS-0213383, SRPT-VYDS-0213393, SRPT-VYDS-0213404. Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted],

[redacted] Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of third-party manufacturing, particularly in light of Sarepta's Response to Interrogatory No. 3, in which Sarepta has indicated that information, including manufacturing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15 (dated April 11, 2022).

Further, as described above, Sarepta directs and controls the testing of golodirsen such that the performance of the testing is attributable to Sarepta. However, to the extent that Sarepta argues that it does not direct or control the testing of golodirsen, but contracts out the testing of golodirsen to another entity, then the testing entity directly infringes the NS Product Claims by using the infringing product (e.g., golodirsen). *See e.g.,* Highlights of Prescribing Information (Dec. 12, 2019) § 12-14 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12-14; SRPT-VYDS-0007020 at -22. Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's testing, particularly in light of Sarepta's Response to Interrogatory No. 10, in which Sarepta has indicated that information, including testing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 21-22 (dated April 11, 2022).

Finally, the medical professionals who administer VYONDYS 53 (golodirsen) and patients to whom VYONDYS 53 (golodirsen) is administered directly infringe the NS Product Claims by using the infringing product. Highlights of Prescribing Information (Dec. 12, 2019) §

2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. Nippon Shinyaku may rely upon Sarepta's marketing and instructional materials instructing medical professionals how to prescribe, dose, formulate, and administer VYONDYS 53 (golodirsen), such as SRPT-VYDS-0212852, SRPT-VYDS-0212977, SRPT-VYDS-0213053. Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted]

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

d. Sarepta Indirectly Infringes the NS Product Claims Under 35 U.S.C. § 271(b)

Sarepta induces and encourages third party manufacturers to directly infringe the NS Product Claims by manufacturing golodirsen [redacted]

[redacted]

SRPT-VYDS-0006997 at -98; *see also* SRPT-VYDS-0213330, SRPT-VYDS-0213333, SRPT-VYDS-0213381, SRPT-VYDS-0213383, SRPT-VYDS-0213393, SRPT-VYDS-0213404. Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted] Accordingly, Sarepta indirectly infringes the NS Product Claims under 35 U.S.C. § 271(b). Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's inducement of third-party manufacturing, particularly in light of Sarepta's Response to Interrogatory No. 3, in which Sarepta has indicated that information, including manufacturing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15 (dated April 11, 2022).

Sarepta induces and encourages third party testing entities to directly infringe the NS Product Claims by testing golodirsen at least [redacted]

[redacted] *See e.g.,* Highlights of Prescribing Information (Dec. 12, 2019) § 12-14 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12-14; SRPT-VYDS-0007020 at -22. Accordingly, Sarepta indirectly infringes the NS Product Claims under 35 U.S.C. § 271(b). Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's inducement of third-party testing, particularly in light of Sarepta's Response to Interrogatory No. 10, in which Sarepta has indicated that information, including testing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 21-22 (dated April 11, 2022).

Sarepta induces and encourages third party medical professionals and patients to directly infringe the NS Product Claims by using VYONDYS 53 (golodirsen) at least by selling VYONDYS 53 (golodirsen) and providing detailed prescribing information that details how and why to administer VYONDYS 53 (golodirsen). Sarepta's sale of VYONDYS 53 (golodirsen) is shown at least by certain sales data produced by Sarepta. *See e.g.,* SRPT-VYDS-0006844–6978; SRPT-VYDS-0007097–7262. Further Sarepta provides prescribing information that includes instruction and encouragement for medical professionals and patients to use VYONDYS 53 (golodirsen) for the treatment of muscular dystrophy:

> "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping."

Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The prescribing information provides instructions as to how VYONDYS 53 (golodirsen) should be administered to a patient intravenously, further demonstrating Sarepta's inducement:

2.4 Administration Instructions

Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered.

VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion.

Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* *SRPT-VYDS-0006978 - Highlights* of Prescribing Information (Feb. 2021) § 2.4. Nippon Shinyaku may rely upon Sarepta's marketing and instructional materials instructing medical professionals how to prescribe, dose, formulate, and administer VYONDYS 53 (golodirsen), such as SRPT-VYDS-0212852, SRPT-VYDS-0212977, SRPT-VYDS-0213053. Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted]

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's inducement of third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement,

particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

Accordingly, Sarepta indirectly infringes the NS Product Claims under 35 U.S.C. § 271(b). Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

e. Sarepta Indirectly Infringes the NS Product Claims Under 35 U.S.C. § 271(c)

Sarepta contributes to third party medical professionals' and patients' direct infringement of the NS Product Claims by using VYONDYS 53 (golodirsen) at least by selling and offering for sale VYONDYS 53 (golodirsen). Sarepta's sale and offer for sale of VYONDYS 53 (golodirsen) is shown at least by certain sales data produced by Sarepta. *See e.g.,* SRPT-VYDS-0006844–6978; SRPT-VYDS-0007097–7262. Nippon Shinyaku may rely upon any and all sales data produced by Sarepta in this case, including [redacted]

Further, VYONDYS 53 (golodirsen) is especially made or adapted for use in infringement and does not have substantial noninfringing uses. Indeed, the prescribing

information for VYONDYS 53 (golodirsen) identifies the only indication as the treatment of DMD by inducing exon 53 skipping:

> "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping."

Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. Nippon Shinyaku may rely upon Sarepta's marketing and instructional materials instructing medical professionals how to prescribe, dose, formulate, and administer VYONDYS 53 (golodirsen), such as SRPT-VYDS-0212852, SRPT-VYDS-0212977, SRPT-VYDS-0213053.

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's contribution to third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

Accordingly, Sarepta indirectly infringes the NS Product Claims under 35 U.S.C. § 271(c). Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

B. Infringement of the NS Method of Use Claims

As set forth in Appendices A5-A6, the administration of VYONDYS 53 (golodirsen)

meets each of the limitations of the NS Method of Use Claims either literally or under the doctrine of equivalents. For the reasons described below, Sarepta directly and/or indirectly infringes each of the NS Method of Use Claims under at least 35 U.S.C. § 271(a), (b), and (c).

1. Sarepta Directly Infringes the NS Method of Use Claims Under 35 U.S.C. § 271(a)

Sarepta directly infringes and will continue to directly infringe the NS Method of Use Claims under 35 U.S.C. § 271(a) by using VYONDYS 53 (golodirsen). Specifically, Sarepta has used VYONDYS 53 (golodirsen) in testing, including clinical testing. *See e.g.,* Highlights of Prescribing Information (Dec. 12, 2019) § 12-14 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12-14. To the extent that Sarepta argues that it does not directly perform the clinical testing of golodirsen, but contracts out the clinical testing of golodirsen to another entity, Sarepta directs and controls the clinical testing of golodirsen such that the performance of the testing is attributable to Sarepta. *Id.* Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's testing, particularly in light of Sarepta's Response to Interrogatory No. 10, in which Sarepta has indicated that information, including testing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 21-22 (dated April 11, 2022).

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta

and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

2. Sarepta Indirectly Infringes the NS Method of Use Claims Under 35 U.S.C. §§ 271(b) and 271(c)

Indirect infringement under both 35 U.S.C. § 271(b) and (c) requires knowledge of the NS Asserted Patents and knowledge of infringement. Both types of indirect infringement also require a third-party direct infringer. Induced infringement under 35 U.S.C. § 271(b) requires that that Sarepta also induce or encourage another party to directly infringe. Contributory infringement under 35 U.S.C. § 271(c) also requires that that Sarepta offer to sell, sell, or import a component that is a material part of an invention that is especially made or adapted for use in infringement, and does not have substantial noninfringing uses. As set forth below, Sarepta induces and contributes to infringement under both 35 U.S.C. § 271(b) and (c).

a. Sarepta Had Knowledge of the NS Asserted Patents

As set forth above in Section II.A.2.a, Sarepta had knowledge of each of the NS Asserted Patents at least as of each of their issuance dates and/or [redacted]

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's knowledge of the NS Asserted Patents and knowledge of infringement, particularly in light of Sarepta's Response to Interrogatory No. 5, in which Sarepta has indicated that information, including information regarding Sarepta's awareness of the NS Asserted Patents will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 17 (dated April 11, 2022).

b. Sarepta Had Knowledge that the Administration of VYONDYS 53 Infringes the NS Asserted Patents

As set forth above, in Section II.A.2.b, Sarepta had knowledge that the sale, offer for sale, importation, use, or manufacture of VYONDYS 53 (golodirsen) would infringe the NS Asserted Patents at least as of each of their issuance dates and/or [redacted]

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's knowledge of the NS Asserted Patents and knowledge of infringement, particularly in light of Sarepta's Response to Interrogatory No. 5, in which Sarepta has indicated that information, including information regarding Sarepta's awareness of the NS Asserted Patents will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 17 (dated April 11, 2022).

c. Third Parties Directly Infringe the NS Method of Use Claims

The medical professionals who administer VYONDYS 53 (golodirsen) directly infringe the NS Method of Use Claims by performing the steps of the NS Method of Use Claims, including intravenously administering VYONDYS 53 (golodirsen). Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

d. Sarepta Indirectly Infringes the NS Method of Use Claims Under 35 U.S.C. § 271(b)

Sarepta induces and encourages third party medical professionals to directly infringe the NS Method of Use Claims by using VYONDYS 53 (golodirsen) at least by selling VYONDYS 53 (golodirsen) and providing detailed prescribing information that details how and why to administer VYONDYS 53 (golodirsen). Sarepta's sale of VYONDYS 53 (golodirsen) is shown at least by certain sales data produced by Sarepta. *See e.g.,* SRPT-VYDS-0006844–6978; SRPT-VYDS-0007097–7262. Nippon Shinyaku may rely upon any and all sales data produced

by Sarepta in this case, including [redacted] Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted]

Further, Sarepta provides prescribing information that includes instruction and encouragement for medical professionals to intravenously administer VYONDYS 53 (golodirsen) for the treatment of muscular dystrophy:

> "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping."

Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The prescribing information provides instructions as to how VYONDYS 53 (golodirsen) should be administered to a patient intravenously, further demonstrating Sarepta's inducement:

2.4 Administration Instructions

Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered.

VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion.

Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 -

Highlights of Prescribing Information (Feb. 2021) § 2.4. Nippon Shinyaku may rely upon Sarepta's marketing and instructional materials instructing medical professionals how to prescribe, dose, formulate, and administer VYONDYS 53 (golodirsen), such as SRPT-VYDS-0212852, SRPT-VYDS-0212977, SRPT-VYDS-0213053.

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's inducement of third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

Accordingly, Sarepta indirectly infringes the NS Method of Use Claims under 35 U.S.C. § 271(b). Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

e. Sarepta Indirectly Infringes the NS Product Claims Under 35 U.S.C. § 271(c)

Sarepta contributes to third party medical professionals' direct infringement of the NS Product Claims by administering VYONDYS 53 (golodirsen) at least by selling VYONDYS 53 (golodirsen). Sarepta's sale of VYONDYS 53 (golodirsen) is shown at least by certain sales data produced by Sarepta. *See e.g.,* SRPT-VYDS-0006844–6978; SRPT-VYDS-0007097–7262. . Nippon Shinyaku may rely upon any and all sales data produced by Sarepta in this case, including [redacted]

[redacted] Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted]

Further, VYONDYS 53 (golodirsen) is especially made or adapted for use in infringement and does not have substantial noninfringing uses. Indeed, the prescribing information for VYONDYS 53 (golodirsen) identifies the only indication as the treatment of DMD by inducing exon 53 skipping:

> "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping."

Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The prescribing information provides instructions as to how VYONDYS 53 (golodirsen) should be administered to a patient intravenously, further demonstrating the lack of any non-infringing use:

2.4 Administration Instructions

Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered.

VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion.

Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 -

Highlights of Prescribing Information (Feb. 2021) § 2.4. Nippon Shinyaku may rely upon Sarepta's marketing and instructional materials instructing medical professionals how to prescribe, dose, formulate, and administer VYONDYS 53 (golodirsen), such as SRPT-VYDS-0212852, SRPT-VYDS-0212977, SRPT-VYDS-0213053.

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's contribution to third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

Accordingly, Sarepta indirectly infringes the NS Method of Use Claims under 35 U.S.C. § 271(c). Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

C. Infringement of the NS Method of Making Claims

As set forth in Appendix A7, the manufacture of VYONDYS 53 (golodirsen) meets each of the limitations of the NS Method of Making Claims either literally or under the doctrine of equivalents. For the reasons described below, Sarepta directly and/or indirectly infringes each of the NS Method of Making Claims under at least 35 U.S.C. § 271(a), (b), and (g).

1. Sarepta Directly Infringes the NS Method of Making Claims Under 35 U.S.C. § 271(a)

Sarepta directly infringes and will continue to directly infringe the NS Method of

Making Claims under 35 U.S.C. § 271(a) by making VYONDYS 53 (golodirsen). Specifically, Sarepta informed that FDA that:

[redacted]

SRPT-VYDS-0006997 at -98. To the extent that Sarepta argues that it does not directly manufacture golodirsen, but contracts out the manufacture of golodirsen to another entity (e.g., [redacted]), Sarepta directs and controls the manufacture of golodirsen such that the performance of every step manufacturing step is attributable to Sarepta. *Id.*; *see also BMC Res., Inc. v. Paymentech, L.P.*, 498 F.3d 1373, 1379-81 (Fed. Cir. 2007); *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318 (Fed. Cir. 2008). Accordingly, Sarepta directly infringes and will contrinue to directly infringe the NS Method of Making Claims under 35 U.S.C. § 271(a) by making VYONDYS 53 (golodirsen). Indeed, the prescribing information for VYONDYS 53 (golodirsen) states that it is:

Manufactured for:
Sarepta Therapeutics, Inc.
Cambridge, MA 02142 USA

Highlights of Prescribing Information (Dec. 12, 2019) § 17 (emphasis added); *see also SRPT-VYDS-0006978 - Highlights* of Prescribing Information (Feb. 2021) § 17. And Sarepta affirmatively holds itself out as "[redacted] Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted]

[redacted]

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's manufacturing, particularly in light of Sarepta's Response to Interrogatory No. 3, in which Sarepta has indicated that information, including manufacturing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15 (dated April 11, 2022).

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's contribution to third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

2. Sarepta Indirectly Infringes the NS Method of Making Claims Under 35 U.S.C. §§ 271(b)

Indirect infringement under 35 U.S.C. § 271(b) requires knowledge of the NS Asserted Patents and knowledge of infringement. Induced infringement under 35 U.S.C. § 271(b) also requires a third-party direct infringer and requires that that Sarepta also induce or encourage another party to directly infringe. As set forth below, Sarepta induces infringement under 35 U.S.C. § 271(b).

a. Sarepta Had Knowledge of the NS Asserted Patents

As set forth above in Section II.A.2.a, Sarepta had knowledge of each of the NS Asserted Patents at least as of each of their issuance dates and/or [redacted]

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's knowledge of the NS Asserted Patents and knowledge of infringement, particularly in light of Sarepta's Response to Interrogatory No. 5, in which Sarepta has indicated that information, including information regarding Sarepta's awareness of the NS Asserted Patents will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 17 (dated April 11, 2022).

b. Sarepta Had Knowledge that the Manufacture of VYONDYS 53 Infringes the NS Asserted Patents

As set forth above, in Section II.A.2.b, Sarepta had knowledge that the sale, offer for sale, importation, use, or manufacture of VYONDYS 53 (golodirsen) would infringe the NS Asserted Patents at least as of each of their issuance dates and/or [redacted]

Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's knowledge of the NS Asserted Patents and knowledge of infringement, particularly in light of Sarepta's Response to Interrogatory No. 5, in which Sarepta has indicated that information, including information regarding Sarepta's awareness of

the NS Asserted Patents will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 17 (dated April 11, 2022).

c. Third Parties Directly Infringe the NS Method of Making Claims

As described above, Sarepta directs and controls the manufacture of golodirsen such that the performance of every step manufacturing step is attributable to Sarepta. However, to the extent that Sarepta argues that it does not direct or control the manufacture of golodirsen, but [redacted] Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of third-party manufacturing, particularly in light of Sarepta's Response to Interrogatory No. 3, in which Sarepta has indicated that information, including manufacturing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15

(dated April 11, 2022).

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

d. Sarepta Indirectly Infringes the NS Method of Making Claims Under 35 U.S.C. § 271(b)

Sarepta induces and encourages third party manufacturers to directly infringe the NS Product Claims by manufacturing golodirsen [redacted]

[redacted]

SRPT-VYDS-0006997 at -98; *see also* SRPT-VYDS-0213330, SRPT-VYDS-0213333, SRPT-VYDS-0213381, SRPT-VYDS-0213383, SRPT-VYDS-0213393, SRPT-VYDS-0213404. [redacted]

[redacted] Accordingly, Sarepta indirectly infringes the NS Method of Making Claims under 35 U.S.C. § 271(b). Nippon Shinyaku reserves the right to supplement or amend these contentions to identify additional evidence of Sarepta's inducement of third-party manufacturing, particularly in light of Sarepta's Response to Interrogatory No. 3, in which Sarepta has indicated that information, including manufacturing information will "be produced in this case on a rolling basis." Sarepta's Responses and Objections to NS's First Set of Interrogatories (Nos. 1-13) at 14-15 (dated April 11, 2022).

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's inducement of third-party acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta and third-party witnesses designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

3. Sarepta Infringes the NS Method of Making Claims Under 35 U.S.C. § 271(g)

Infringement under 35 U.S.C. § 271(g) requires proof that a party imports, offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States. As set forth in Appendix A7, the NS Method of Making Claims cover the manufacture of golodirsen, the active ingredient in VYONDYS 53 (golodirsen). Accordingly, Sarepta infringes 35 U.S.C. § 271(g) by selling and/or offering to sell VYONDYS 53 (golodirsen). Sarepta's offers for sale and/or sale of VYONDYS 53 (golodirsen) is shown at least by certain sales data produced by Sarepta. *See e.g.,* SRPT-VYDS-0006844–6978; SRPT-VYDS-0007097–7262. Nippon Shinyaku may rely upon any and all sales data produced by Sarepta in this case, including [redacted] Nippon Shinyaku may further rely upon evidence relating to Sarepta's [redacted]

Nippon Shinyaku may rely upon Sarepta's admissions made in pleadings, responses to interrogatories and requests for admission (particularly Sarepta's responses to Interrogatory Nos. 3, 10, 20, and 21 which have not been supplemented to date), as further evidence of Sarepta's acts of direct infringement. Nippon Shinyaku likewise notes that depositions are ongoing, and that it may rely upon the testimony of Sarepta's, Nippon Shinyaku's, and NS Pharma's witnesses as yet further evidence of Sarepta's infringement, particularly testimony by Sarepta witnesses

designated to testify under Fed. R. Civ. P. 30(b)(6) regarding supply chain, marketing, sales, distribution, prescribing, administration and manufacturing-related topics.

[redacted] Thus, Sarepta has infringed and continues to infringe the NS Method of Making Claims under 35 U.S.C. § 271(g). Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

D. Sarepta Has Willfully Infringed the NS Asserted Patents

As set forth above in Section II.A.2.a, Sarepta had knowledge of each of the NS Asserted Patents at least as of each of their issuance dates and/or [redacted] As set forth above, in Section II.A.2.b, Sarepta had knowledge that the sale, offer for sale, importation, use, or manufacture of VYONDYS 53 (golodirsen) would infringe the NS Asserted Patents at least as of each of their issuance dates and/or [redacted] Yet, despite this knowledge, and as set forth herein, Sarepta continues to a continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the NS Asserted Patents, and in doing so knew or should have known that its conduct amounted to infringement. Accordingly, Sarepta is liable for willful infringement of the NS Asserted Patents. Nippon Shinyaku reserves the right to supplement or amend these contentions as discovery in this case proceeds.

Dated: July 27, 2023

Respectfully submitted,

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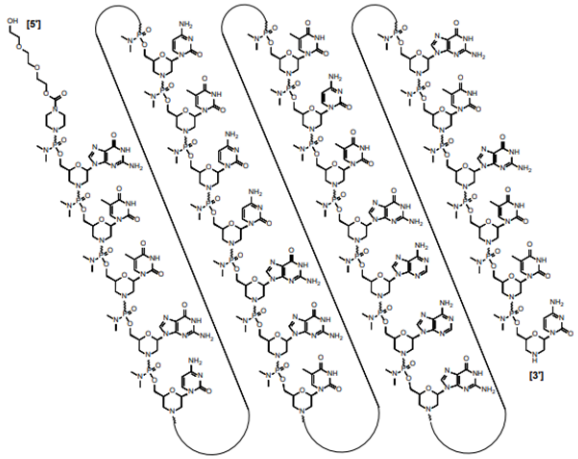
Appendix A1

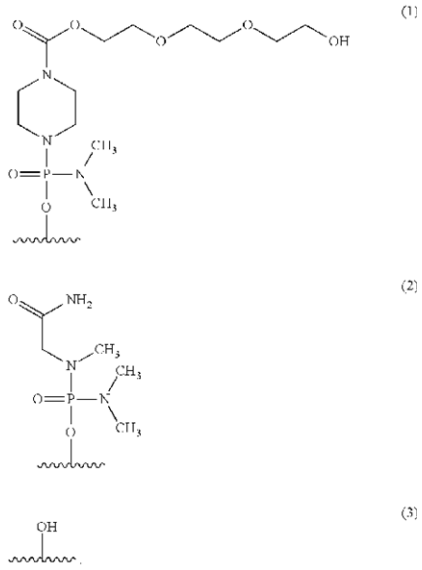
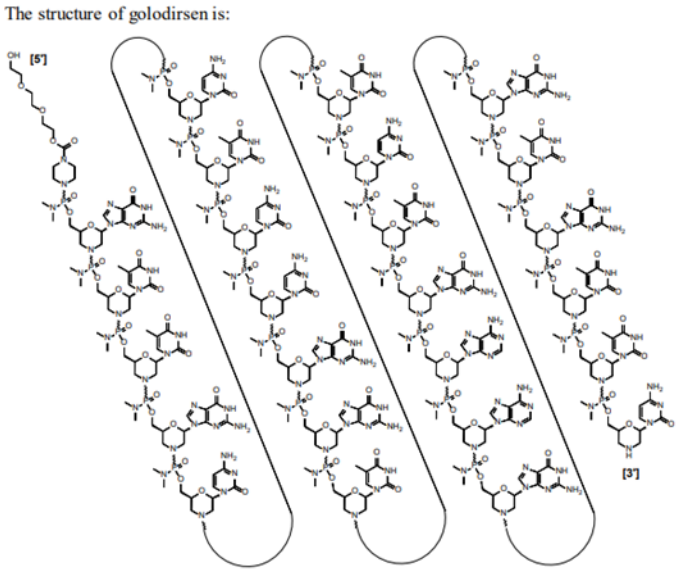
Infringement Chart for US 9,708,361

Claim #	Lim #	Limitation	Evidence
1	a	An antisense oligomer	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an antisense oligomer: "Golodirsen is an **antisense oligonucleotide** of the phosphorodiamidate morpholino **oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	b	which causes skipping of the 53rd exon in the human dystrophin gene	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
1	c	consisting of the nucleotide sequence of SEQ ID NO: 57	SEQ ID NO 57 is: GUUGCCUCCGGUUCUGAAGGUGUUC VYONDYS 53 (golodirsen) contains golodirsen, which is an antisense oligomer of the following nucleotide sequence:

Claim #	Lim #	Limitation	Evidence
			GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. This sequence is identical to SEQ ID NO 57, except that the uracil bases in SEQ ID NO 57 have been replaced with equivalent thymine bases in VYONDYS 53 (golodirsen), that are not substantially different. The thymine bases in VYONDYS 53 (golodirsen) perform the same function, in the same way, to achieve the same result as the uracil bases in SEQ ID NO 57. Accordingly, VYONDYS 53 (golodirsen) meets this limitation under at least the doctrine of equivalents.
1	d	wherein the antisense oligomer is an oligonucleotide in which the sugar moiety and/or the phosphate-binding region of at least one nucleotide constituting the oligonucleotide is modified, or a morpholino oligomer.	VYONDYS 53 (golodirsen) includes oligonucleotides in which the sugar moiety and/or the phosphate-binding region is modified, or a morpholino oligomer: "Golodirsen is an antisense oligonucleotide of the ***phosphorodiamidate morpholino oligomer*** (PMO) subclass. PMOs are synthetic molecules ***in which the five-membered ribofuranosyl rings found in natural DNA and RNA are replaced by a six-membered morpholino ring***. Each morpholino ring is linked through an uncharged phosphorodiamidate moiety rather than the negatively charged phosphate linkage that is present in natural DNA and RNA." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	a	The antisense oligomer according to claim 1,	See claim 1.
3	b	wherein the phosphate-binding region of at least one nucleotide constituting the oligonucleotide is any one selected from the group	VYONDYS 53 (golodirsen) includes oligonucleotides in which the phosphate-binding region is a phosphoramidate bond:

Claim #	Lim #	Limitation	Evidence
		consisting of: a phosphorothioate bond, a phosphorodithioate bond, an alkylphosphonate bond, a phosphoramidate bond, and a boranophosphate bond.	"Golodirsen is an antisense oligonucleotide of the ***phosphorodiamidate morpholino oligomer*** (PMO) subclass. PMOs are synthetic molecules in which the five-membered ribofuranosyl rings found in natural DNA and RNA are replaced by a six-membered morpholino ring. Each morpholino ring is linked through ***an uncharged phosphorodiamidate moiety*** rather than the negatively charged phosphate linkage that is present in natural DNA and RNA." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The phosphoramidate bond is also shown in the structure of VYONDYS 53 (golodirsen): The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
4	a	The antisense oligomer according to claim 1,	See claim 1.

Claim #	Lim #	Limitation	Evidence
4	b	which is a morpholino oligomer.	VYONDYS 53 (golodirsen) is a morpholino oligomer: "Golodirsen is an antisense oligonucleotide of the phosphorodiamidate ***morpholino oligomer*** (PMO) subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
5	a	The antisense oligomer according to claim 4,	See claim 4.
5	b	which is a phosphorodiamidate morpholino oligomer.	VYONDYS 53 (golodirsen) is a phosphorodiamidate morpholino oligomer: "Golodirsen is an antisense oligonucleotide of the ***phosphorodiamidate morpholino oligomer*** (PMO) subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
6	a	The antisense oligomer according to claim 4,	See claim 4.

Claim #	Lim #	Limitation	Evidence
6	b	wherein the 5′ end is any one of the groups of chemical formulae (1) to (3) below:  .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the claimed formula 1, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
7	a	A pharmaceutical composition	VYONDYS 53 (golodirsen) injection is a pharmaceutical composition that requires dilution prior to administration: "VYONDYS 53 is supplied in single-dose vials as a preservative-free concentrated solution that requires dilution prior to administration." Highlights of Prescribing Information (Dec. 12, 2019) § 2.3; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.3.
7	b	for the treatment of muscular dystrophy,	VYONDYS 53 (golodirsen) is indicated and administered for the treatment of muscular dystrophy:

Claim #	Lim #	Limitation	Evidence
			"VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. "In the VYONDYS 53 clinical development program, 58 patients received at least one intravenous dose of VYONDYS 53, ranging between 4 mg/kg (0.13 times the recommended dosage) and 30 mg/kg (the recommended dosage). All patients were male and had genetically confirmed Duchenne muscular dystrophy." Highlights of Prescribing Information (Dec. 12, 2019) § 6.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 6.1. "After treatment with VYONDYS 53, all patients evaluated (n=25) in Study 1 Part 2 [see Clinical Studies (14)] had an increase in skipping of exon 53 demonstrated by reverse transcription polymerase chain reaction (RT-PCR), compared to baseline." Highlights of Prescribing Information (Dec. 12, 2019) § 12.2; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.2.
7	c	comprising as an active ingredient the antisense oligomer according to claim 1, or a pharmaceutically acceptable salt or hydrate thereof.	VYONDYS 53 (golodirsen) contains golodirsen, an antisense oligonucleotide, as the active ingredient: "Each milliliter of VYONDYS 53 contains: 50 mg golodirsen; 0.2 mg potassium chloride; 0.2 mg potassium phosphate monobasic; 8 mg sodium chloride; and 1.14 mg sodium phosphate dibasic, anhydrous, in water for injection. . . . Golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown in Claim 1 above, golodirsen meets all of the limitations of claim 1 either literally or under the doctrine of limitations, demonstrating that VYONDYS 53 (golodirsen) meets this limitation.

Appendix A2

Infringement Chart for US 10,385,092

Claim #	Lim #	Limitation	Evidence
1	a	A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO) antisense oligomer: "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	b	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
1	c	consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC.

Claim #	Lim #	Limitation	Evidence
		the 5′ end of the 53rd exon in said human dystrophin pre-mRNA,	’361 Patent at Col. 47, SEQ ID 1; ’361 Patent at Col. 6:38-39 (“The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1.”); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the ’361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5′ end to the 3′ end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 (“Golodirsen contains 25 linked subunits.”); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5′ end of the 53rd exon in human dystrophin pre-mRNA.
1	d	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* ’361 Patent at Col. 47, SEQ ID 1; ’361 Patent at Col. 6:38-39 (“The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1.”); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the ’361 Patent.
1	e	and wherein said PMO antisense oligomer hybridizes to said pre-mRNA with Watson-Crick base	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions:

Claim #	Lim #	Limitation	Evidence
		pairing under physiological conditions.	"Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1  Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
			The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

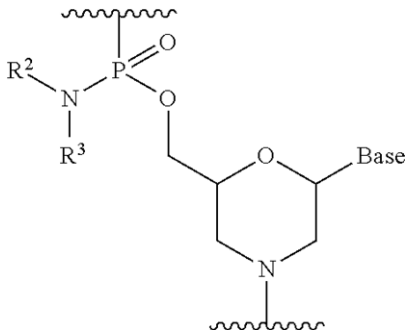
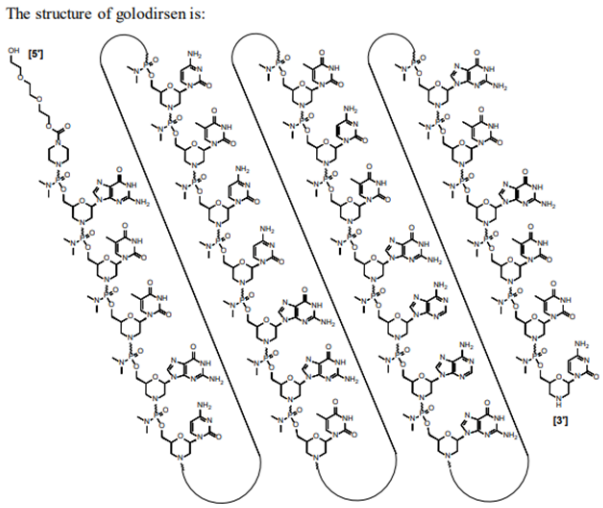
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
2	a	A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO) antisense oligomer: "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	b	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping.

Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
2	c	consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in said human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
2	d	wherein the 53rd exon in said human dystrophin pre-mRNA	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type

Claim #	Lim #	Limitation	Evidence
		consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
2	e	wherein said PMO antisense oligomer hybridizes to said pre-mRNA with Watson-Crick base pairing under physiological conditions,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1  Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end:

Claim #	Lim #	Limitation	Evidence
			GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously:

Claim #	Lim #	Limitation	Evidence
			2.4 Administration Instructions Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]

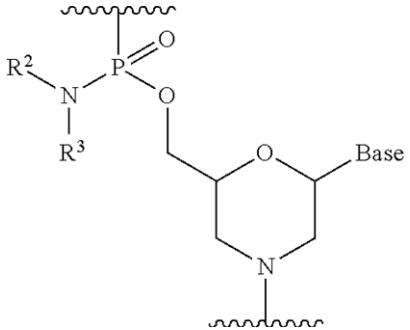
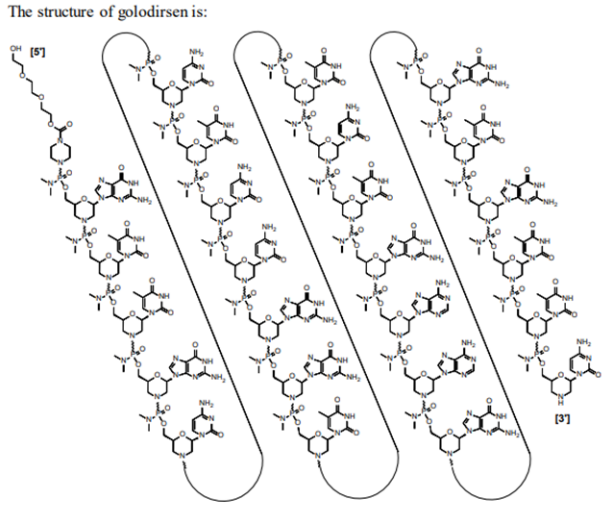
Claim #	Lim #	Limitation	Evidence
2	f	wherein each phosphorodiamidate morpholino monomer of said PMO antisense oligomer has the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	g	wherein Base is a nucleobase selected from the group consisting of cytosine, thymine, adenine, and guanine.	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	a	A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO) antisense oligomer: "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec.

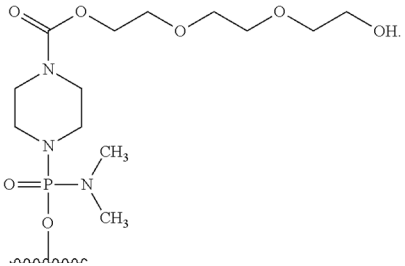
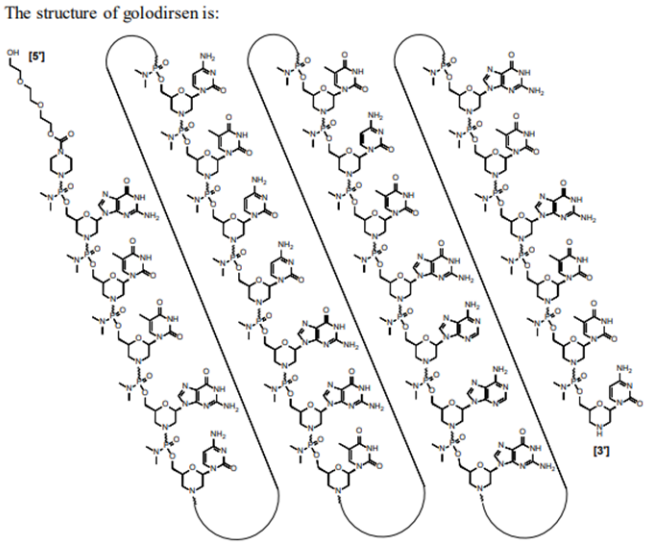
Claim #	Lim #	Limitation	Evidence
			12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	b	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
3	c	consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in said human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end:

Claim #	Lim #	Limitation	Evidence
			GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
3	d	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
3	e	wherein said PMO antisense oligomer hybridizes to said pre-mRNA with Watson-Crick base pairing under physiological conditions,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)).

Claim #	Lim #	Limitation	Evidence
			In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]

Claim #	Lim #	Limitation	Evidence
3	f	wherein each phosphorodiamidate morpholino monomer of said PMO antisense oligomer has the formula:  wherein each of R2 and R3 represents a methyl;	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	g	wherein Base is a nucleobase selected from the group consisting of cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
3	h	wherein the 5’ end of said PMO antisense oligomer has the formula:  .	The 5’ end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below: The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Appendix A3

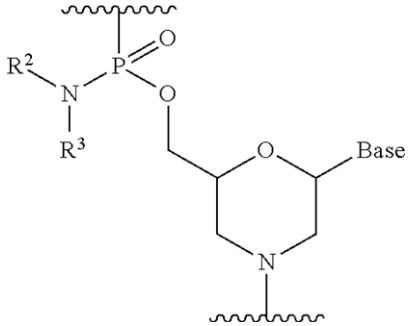
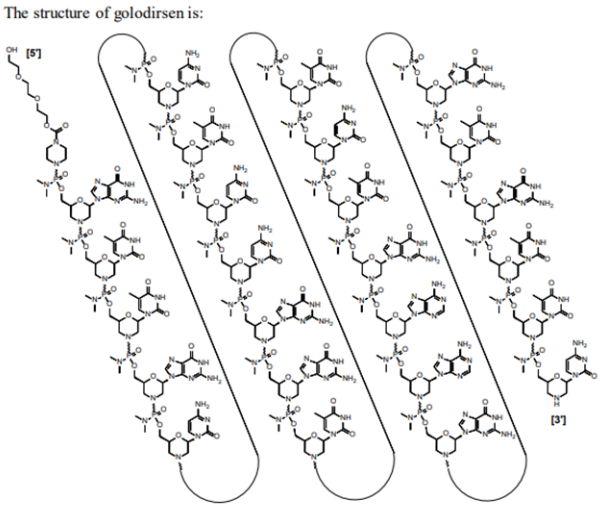
Infringement Chart for US 10,407,461

Claim #	Lim #	Limitation	Evidence
1	a	A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO) antisense oligomer: "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	b	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
1	c	consisting of a 25-mer oligomer that is 100% complementary to the target sequence 5'-	VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end:

Claim #	Lim #	Limitation	Evidence
		GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124) of said human dystrophin pre-mRNA,	GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
1	d	wherein said PMO antisense oligomer hybridizes to said target sequence with Watson-Crick base pairing under physiological conditions,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See*

Claim #	Lim #	Limitation	Evidence
			https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683 Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]

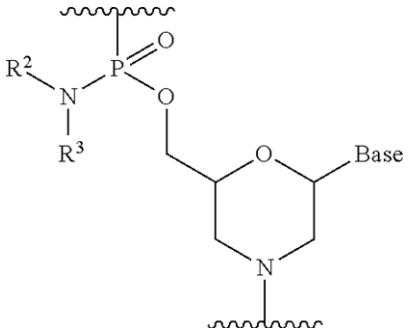
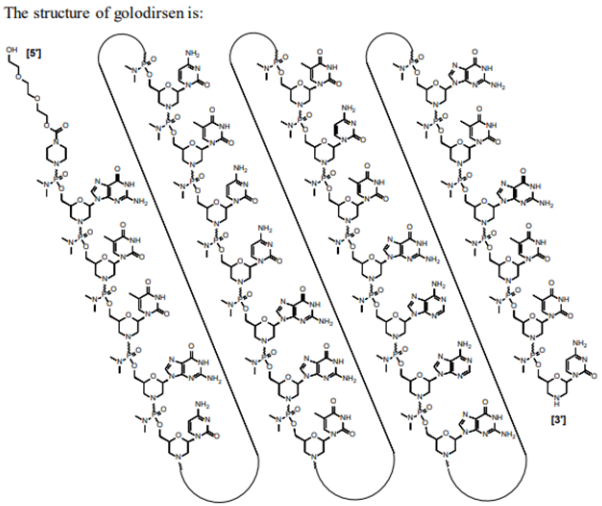
Claim #	Lim #	Limitation	Evidence
1	e	wherein each phosphorodiamidate morpholino monomer of said PMO antisense oligomer has the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	f	wherein Base is a nucleobase selected from the group consisting of uracil, cytosine, thymine, adenine, and guanine.	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	a	A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO) antisense oligomer:

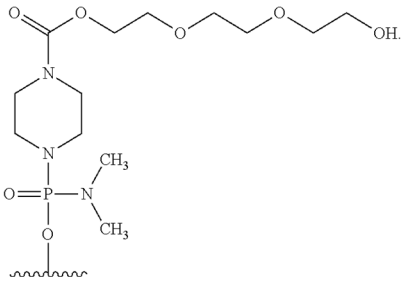
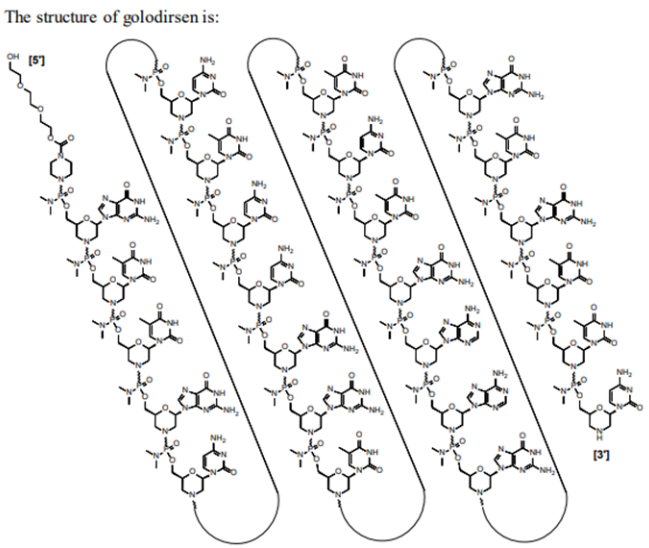
Claim #	Lim #	Limitation	Evidence
			"Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	b	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
2	c	consisting of a 25-mer oligomer that is 100% complementary to the target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124) of said human dystrophin pre-mRNA,	VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
			As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
2	d	wherein said PMO antisense oligomer hybridizes to said target sequence with Watson-Crick base pairing under physiological conditions,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted]

Claim #	Lim #	Limitation	Evidence
			Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing.

Claim #	Lim #	Limitation	Evidence
			Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]

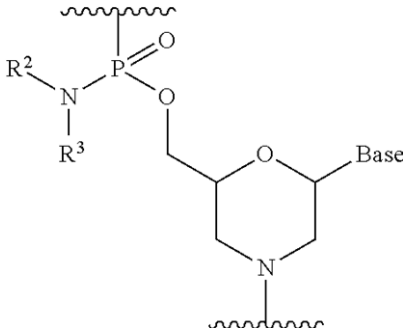
Claim #	Lim #	Limitation	Evidence
2	e	wherein each phosphorodiamidate morpholino monomer of said PMO antisense oligomer has the formula:  wherein each of R2 and R3 represents a methyl;	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	f	wherein Base is a nucleobase selected from the group consisting of uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

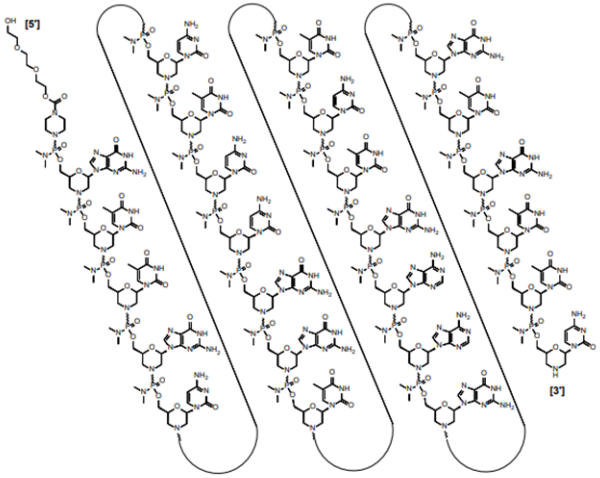
Claim #	Lim #	Limitation	Evidence
2	g	wherein the 5′ end of said PMO antisense oligomer has the formula:  .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

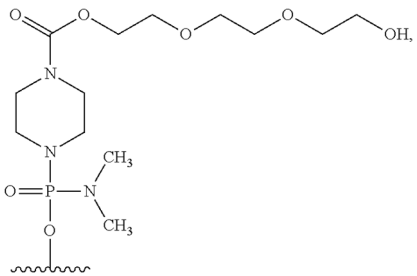
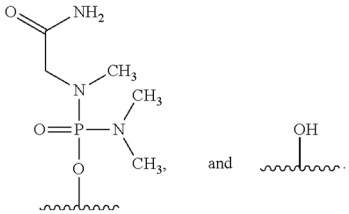
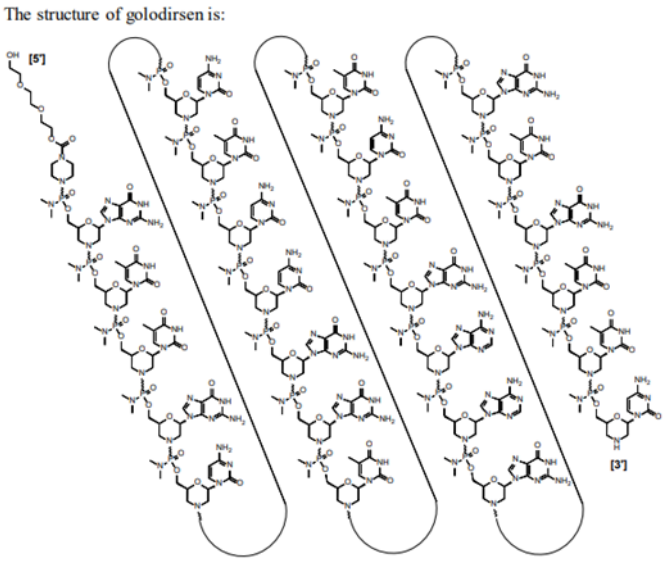
Appendix A4

Infringement Chart for US 10,487,106

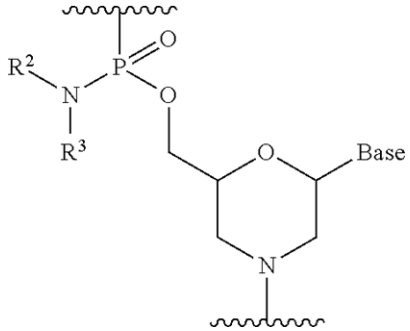
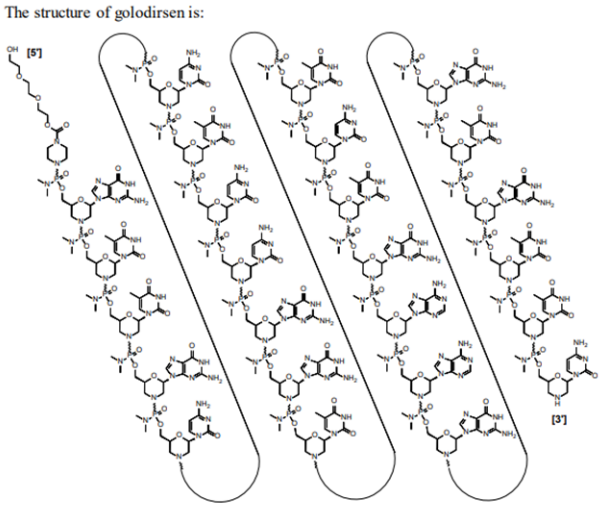
Claim #	Lim #	Limitation	Evidence
1	a	A phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	b	consisting of a 25-mer antisense oligomer that is 100% complementary, according to Watson-Crick base pairing, to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

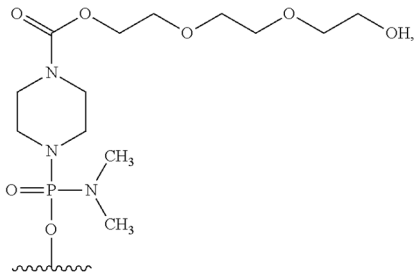
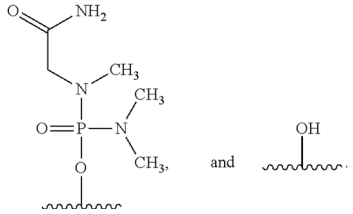
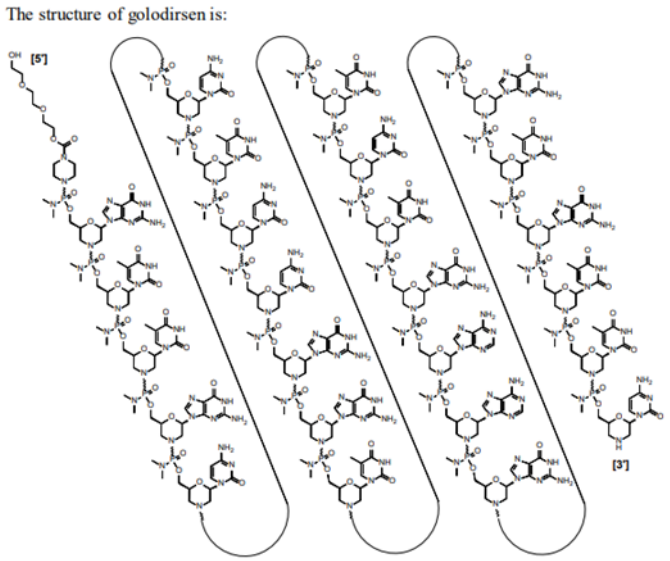
Claim #	Lim #	Limitation	Evidence
			The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
1	c	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
1	d	wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:  wherein each of R2 and R3 represents a methyl;	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):

Claim #	Lim #	Limitation	Evidence
			The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	e	wherein Base is a nucleobase selected from the group consisting of cytosine, thymine, adenine, and guanine, and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
1	f	wherein the 5′ end of said PMO has a formula selected from the group consisting of:   .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula of the first group identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	a	A phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): “Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass.” Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
2	b	consisting of a 25-mer antisense oligomer that is 100% complementary, according to Watson-Crick base pairing, to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
2	c	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is

Claim #	Lim #	Limitation	Evidence
			represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
2	d	wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:  wherein each of R2 and R3 represents a methyl;	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	e	wherein Base is a nucleobase selected from the group consisting of uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
2	f	wherein the 5′ end of said PMO has a formula selected from the group consisting of:   and .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula of the first group identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Appendix A5

Infringement Chart for US 10,647,741

Claim #	Lim #	Limitation	Evidence
1	a	A method comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method comprising administering VYONDYS 53 (golodirsen) to a patient: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
1	b	administering to a patient with DMD	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously:

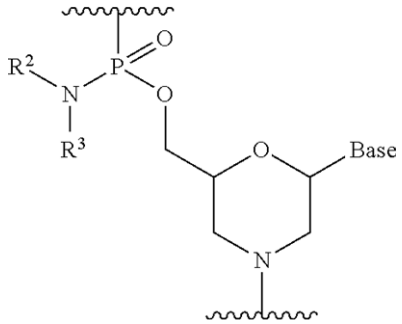
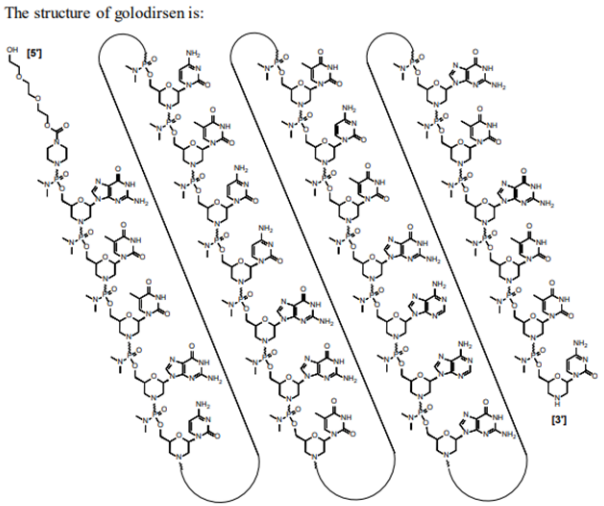
Claim #	Lim #	Limitation	Evidence
			2.4 Administration Instructions Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
1	c	an antisense phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an antisense phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	d	consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end:

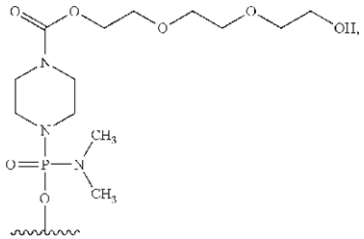
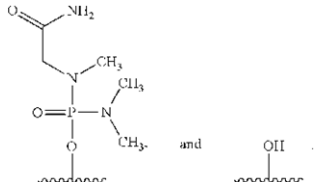
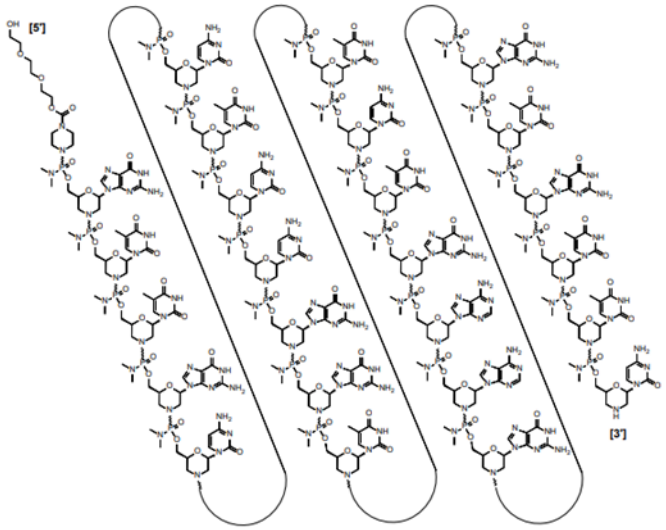
Claim #	Lim #	Limitation	Evidence
			GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
1	e	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
1	f	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing, and	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures

Claim #	Lim #	Limitation	Evidence
			from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.

Claim #	Lim #	Limitation	Evidence
			[redacted]
1	g	wherein skipping of the 53rd exon is induced in said patient.	The administration of VYONDYS 53 (golodirsen) induces skipping of the 53rd exon in patient: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
2	a	The method according to claim 1,	See claim 1.

Claim #	Lim #	Limitation	Evidence
2	b	wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	c	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine.	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	a	The method according to claim 2,	See claim 2.

Claim #	Lim #	Limitation	Evidence
3	b	wherein the 5′ end of said PMO has a formula selected from the group consisting of:   and .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula of the first group identified in the claim, as shown in the structure below: The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
4	a	A method of inducing exon 53 skipping in a patient with DMD comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of inducing exon 53 skipping in a patient: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*.

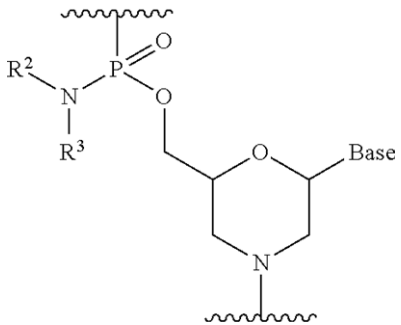
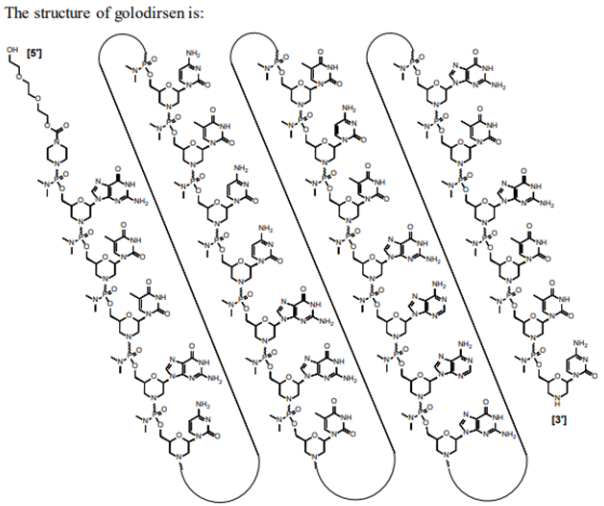
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1. VYONDYS 53 (golodirsen) is administered to patients with DMD: **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
4	b	administering to said patient	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.

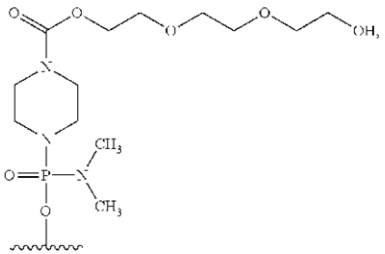
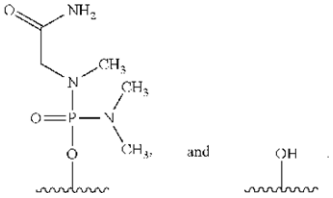
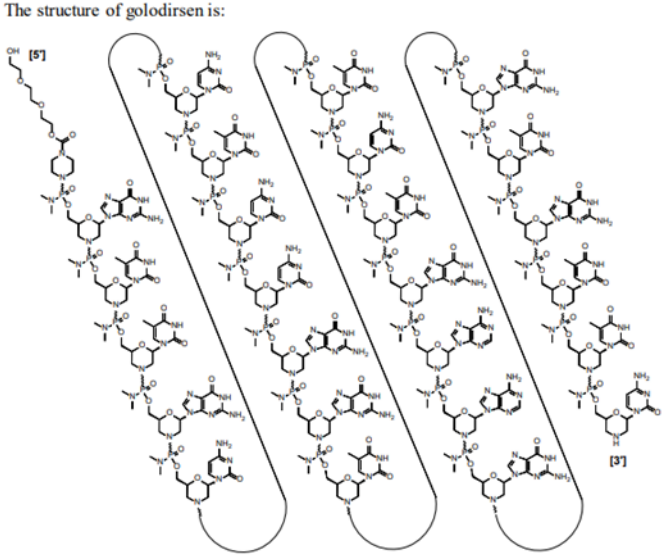
Claim #	Lim #	Limitation	Evidence
4	c	an antisense phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an antisense phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
4	d	consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
			As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
4	e	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, and	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
4	f	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing.	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683*

Claim #	Lim #	Limitation	Evidence
			Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
5	a	The method according to claim 4,	See claim 4.

Claim #	Lim #	Limitation	Evidence
5	b	wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
5	c	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine.	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
6	a	The method according to claim 5,	See claim 5.

Claim #	Lim #	Limitation	Evidence
6	b	wherein the 5′ end of said PMO has a formula selected from the group consisting of:   and .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula of the first group identified in the claim, as shown in the structure below: The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
7	a	A method comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method comprising administering VYONDYS 53 (golodirsen) to a patient: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

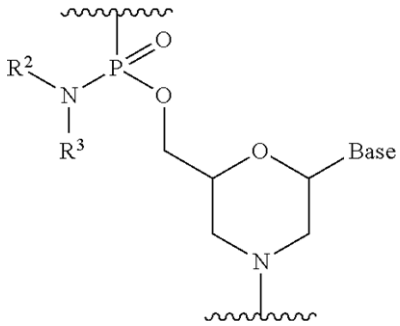
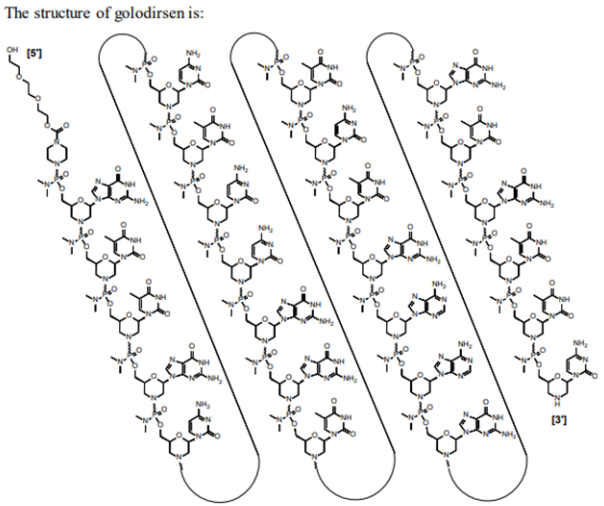
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
7	b	administering to a patient with DMD	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
7	c	an antisense phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an antisense phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis

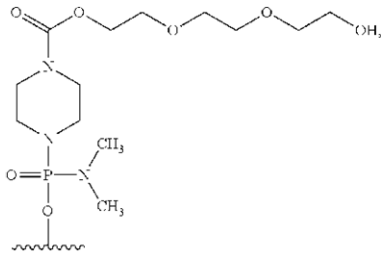
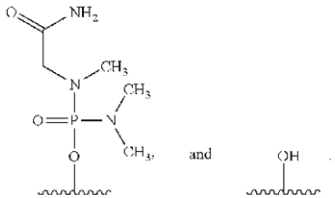
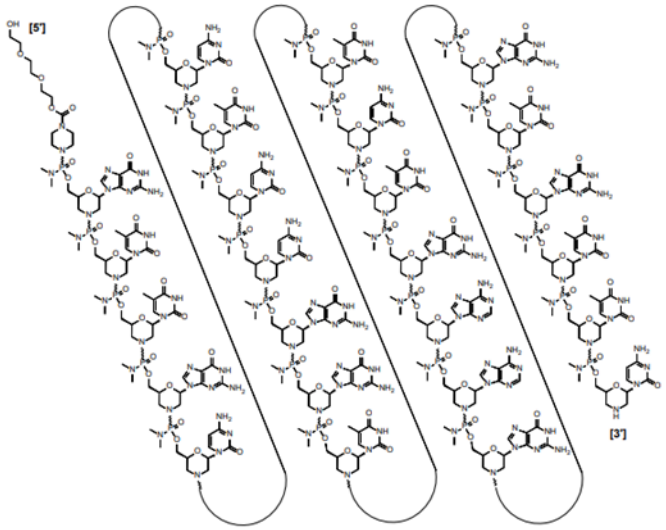
Claim #	Lim #	Limitation	Evidence
			added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
7	d	consisting of a 25-mer oligomer that is 100% complementary to the target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124),	VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
7	e	wherein the 53rd exon in a human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
7	f	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1

Claim #	Lim #	Limitation	Evidence
			 Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC.

Claim #	Lim #	Limitation	Evidence
			'361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
7	g	and wherein skipping of the 53rd exon is induced in said patient.	The administration of VYONDYS 53 (golodirsen) induces skipping of the 53rd exon in patient: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
8	a	The method according to claim 7,	See claim 7.

Claim #	Lim #	Limitation	Evidence
8	b	wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
8	c	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine.	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
9	a	The method according to claim 8,	See claim 8.

Claim #	Lim #	Limitation	Evidence
9	b	wherein the 5' end of said PMO has a formula selected from the group consisting of:   and .	The 5' end of the PMO in VYONDYS 53 (golodirsen) matches the formula of the first group identified in the claim, as shown in the structure below: The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
10	a	A method of inducing exon 53 skipping in a patient with DMD comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of inducing exon 53 skipping in a patient: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*.

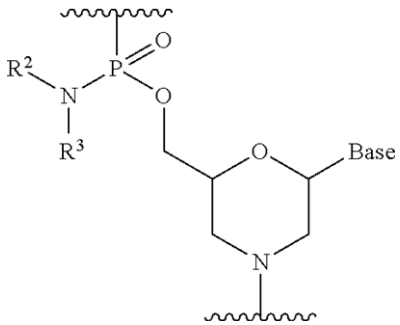
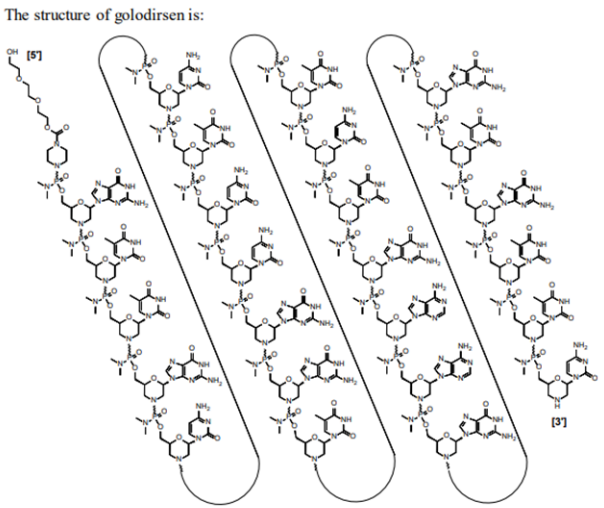
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1. VYONDYS 53 (golodirsen) is administered to patients with DMD: **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
10	b	administering to said patient	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.

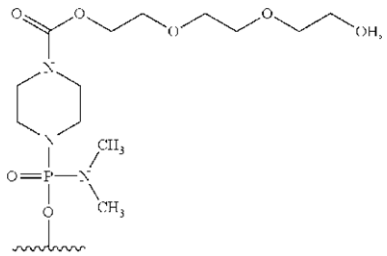
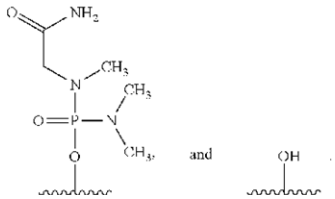
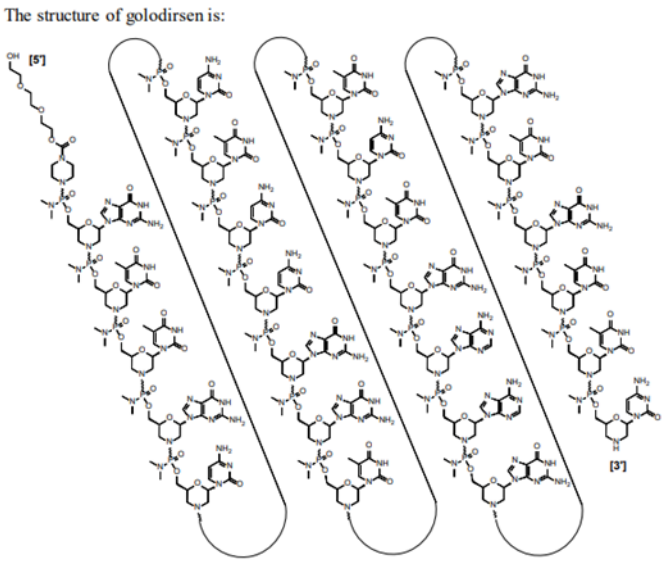
Claim #	Lim #	Limitation	Evidence
10	c	an antisense phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an antisense phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an **antisense oligonucleotide** of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
10	d	consisting of a 25-mer oligomer that is 100% complementary to the target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124),	VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
10	e	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, and	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.

Claim #	Lim #	Limitation	Evidence
10	f	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing.	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end:

Claim #	Lim #	Limitation	Evidence
			GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously:

Claim #	Lim #	Limitation	Evidence
			2.4 Administration Instructions Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
11	a	The method according to claim 10,	See claim 10.

Claim #	Lim #	Limitation	Evidence
11	b	wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
11	c	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine.	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
12	a	The method according to claim 11,	See claim 11.

Claim #	Lim #	Limitation	Evidence
12	b	wherein the 5′ end of said PMO has a formula selected from the group consisting of:   and .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula of the first group identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Appendix A6

Infringement Chart for US 10,662,217

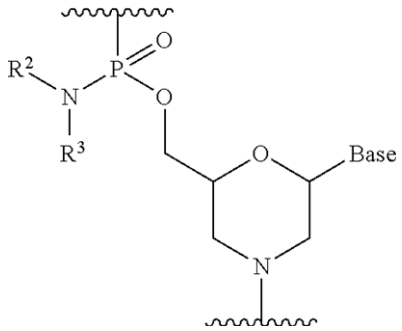
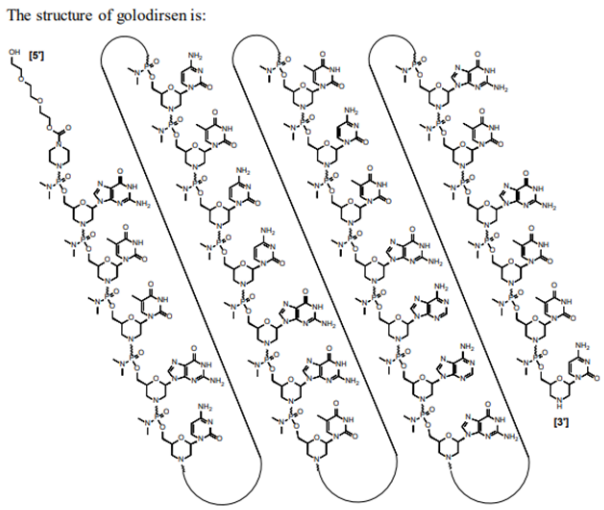
Claim #	Lim #	Limitation	Evidence
1	a	A method of treating a DMD patient comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of treating a DMD patient: **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
1	b	intravenously administering to said patient	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

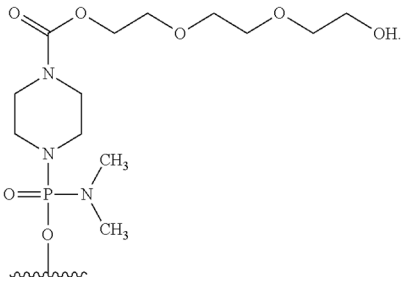
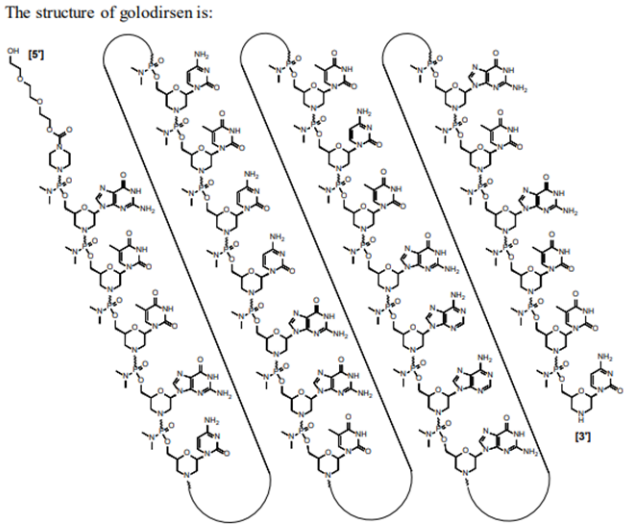
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
1	c	an oligomer comprising:	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an oligomer: "Golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino **oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	d	a) a phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	e	that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)).

Claim #	Lim #	Limitation	Evidence
			VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
1	f	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
1	g	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-*

Claim #	Lim #	Limitation	Evidence
			642-11274-4_1683 (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.

Claim #	Lim #	Limitation	Evidence
			[redacted]
1	h	wherein the phosphorodiamidate morpholino monomers of said PMO have the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

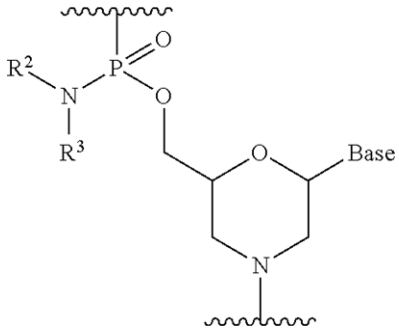
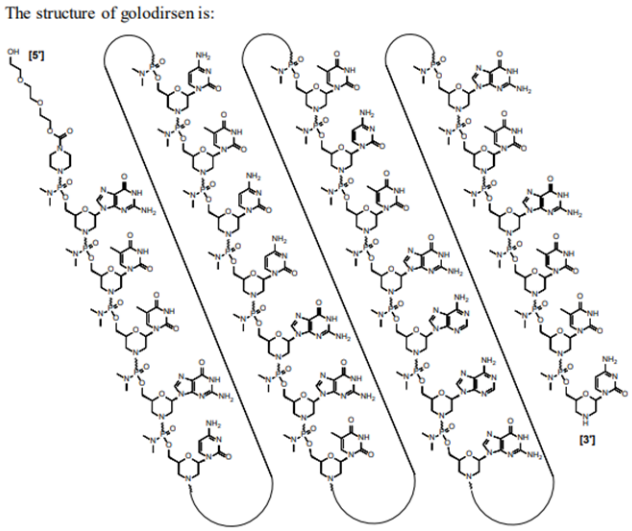
Claim #	Lim #	Limitation	Evidence
1	i	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	j	b) a group at the 5' end of said PMO with the formula: 	The 5' end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	a	A method of treating a DMD patient comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of treating a DMD patient:

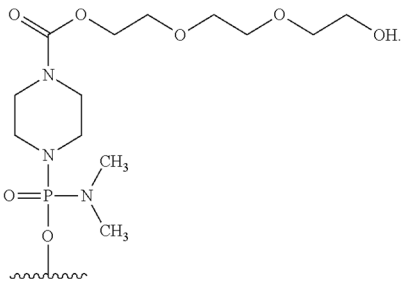
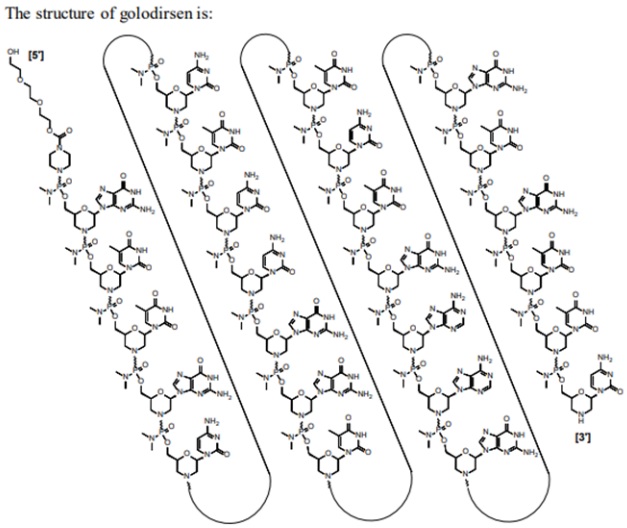
Claim #	Lim #	Limitation	Evidence
			1 INDICATIONS AND USAGE VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
2	b	intravenously administering to said patient	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
2	c	an oligomer comprising:	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an oligomer: "Golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino **oligomer (PMO)** subclass." Highlights of Prescribing

Claim #	Lim #	Limitation	Evidence
			Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	d	a) a phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	e	that is 100% complementary to the target sequence (SEQ ID NO: 124) 5'-GAACACCUUCAGAACCGGAGGCAAC-3' of a human dystrophin pre-mRNA,	VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the target sequence.
2	f	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1

Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC.

Claim #	Lim #	Limitation	Evidence
			'361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
2	g	wherein 25 of the phosphorodiamidate morpholino monomers of said PMO have the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen): 

Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	h	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
2	i	b) a group at the 5' end of said PMO with the formula:  .	The 5' end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below: 

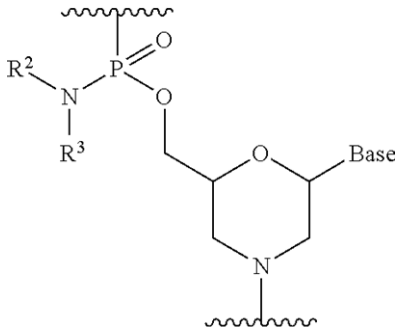
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	a	A method of treating a DMD patient comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of treating a DMD patient: **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
3	b	intravenously administering to said patient	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy: "VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

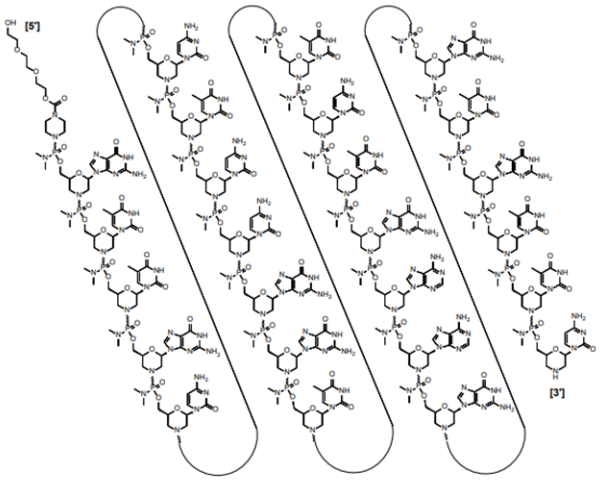
Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
3	c	a phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	d	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA: **12.1 Mechanism of Action** Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
3	e	consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in said human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC.

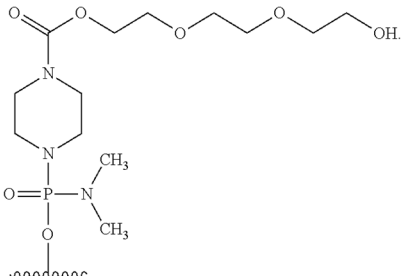
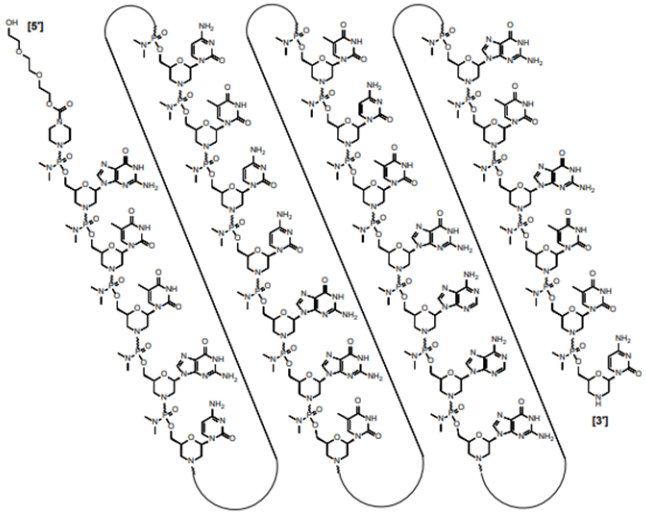
Claim #	Lim #	Limitation	Evidence
			'361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
3	f	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.

Claim #	Lim #	Limitation	Evidence
3	g	wherein said morpholino oligomer hybridizes to said pre-mRNA with Watson-Crick base pairing,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end:

Claim #	Lim #	Limitation	Evidence
			GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously:

Claim #	Lim #	Limitation	Evidence
			2.4 Administration Instructions Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
3	h	wherein each morpholino monomer has the formula:  wherein R2 and R3 are methyl;	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):

Claim #	Lim #	Limitation	Evidence
			The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
3	i	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

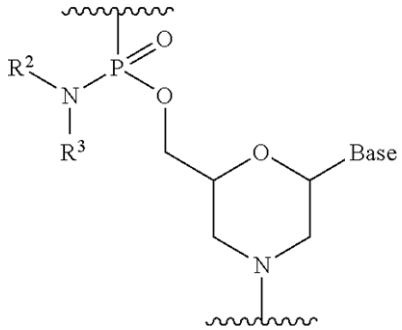
Claim #	Lim #	Limitation	Evidence
3	j	wherein the 5′ end of said PMO has the formula:  .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below: The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
4	a	A method of treating a DMD patient comprising	The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of treating a DMD patient: **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
4	b	intravenously administering to said patient	VYONDYS 53 (golodirsen) is indicated and administered intravenously for the treatment of muscular dystrophy:

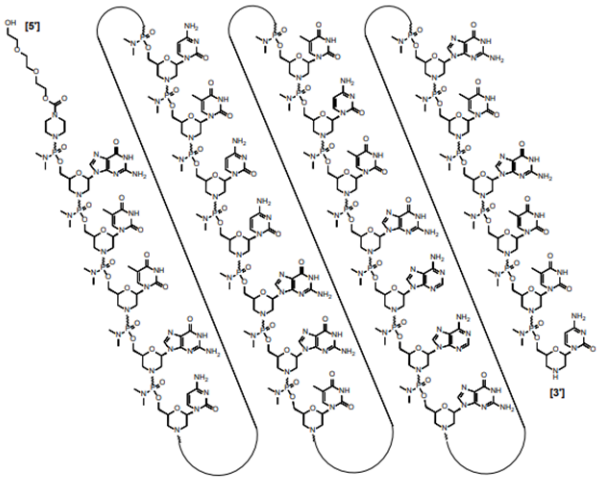
Claim #	Lim #	Limitation	Evidence
			"VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1. The medical professionals and/or other individuals that administer VYONDYS 53 (golodirsen) practice a method of administering VYONDYS 53 (golodirsen) to a patient intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.
4	c	a phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
4	d	that causes skipping of the 53rd exon in a human dystrophin pre-mRNA,	The administration of VYONDYS 53 (golodirsen) includes administering golodirsen, which causes skipping of the 53rd exon in the human dystrophin gene or in a human dystrophin pre-mRNA:

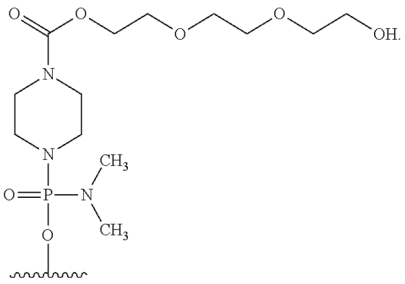
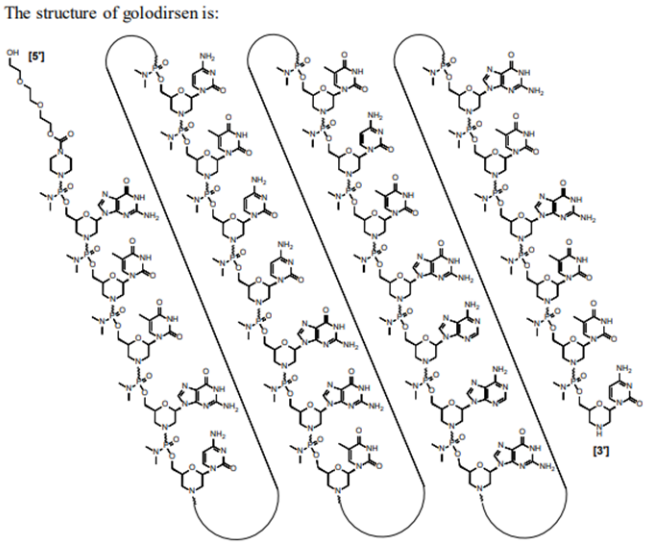
Claim #	Lim #	Limitation	Evidence
			12.1 Mechanism of Action Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping *[see Clinical Studies (14)]*. Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.1. **1 INDICATIONS AND USAGE** VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Highlights of Prescribing Information (Dec. 12, 2019) § 1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 1.
4	e	consisting of a 25-mer oligomer that is 100% complementary to the target pre-mRNA sequence (add SEQ ID NO: 124) 5'-GAACACCUUCAGAACCGGAGGCAAC-3',	VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The sequence of golodirsen consists of 25 nucleotide bases. Highlights of Prescribing Information (Dec. 12, 2019) § 11 ("Golodirsen contains 25 linked subunits."); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
4	g	wherein said morpholino oligomer hybridizes to said pre-mRNA with Watson-Crick base pairing,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions:

Claim #	Lim #	Limitation	Evidence
			"Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1  Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
			The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously:

Claim #	Lim #	Limitation	Evidence
			2.4 Administration Instructions Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
4	h	wherein each morpholino monomer has the formula:  wherein R2 and R3 are methyl;	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):

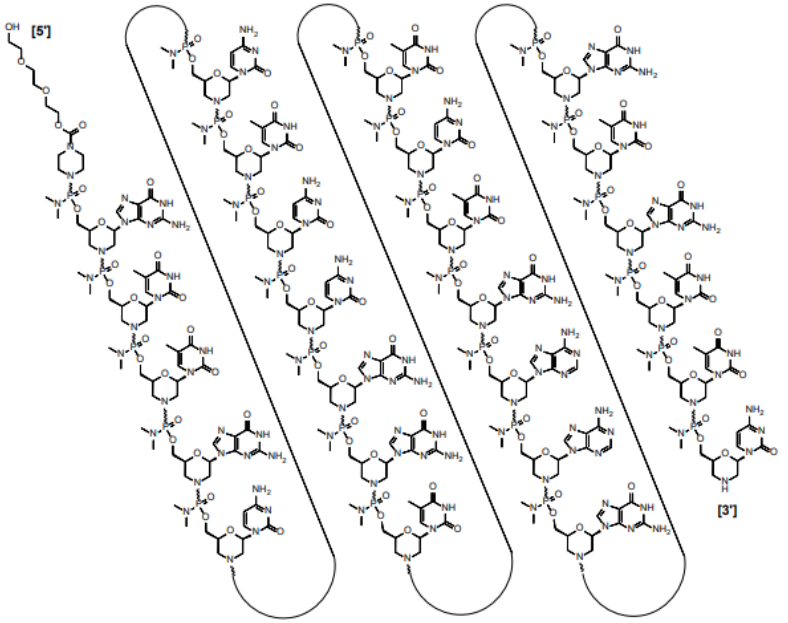
Claim #	Lim #	Limitation	Evidence
			The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
4	i	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
4	j	wherein the 5′ end of said PMO has the formula:  .	The 5′ end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Appendix A7

Infringement Chart for US 10,683,322

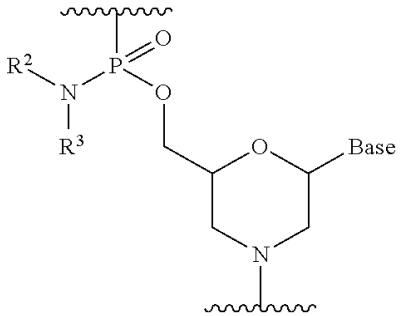
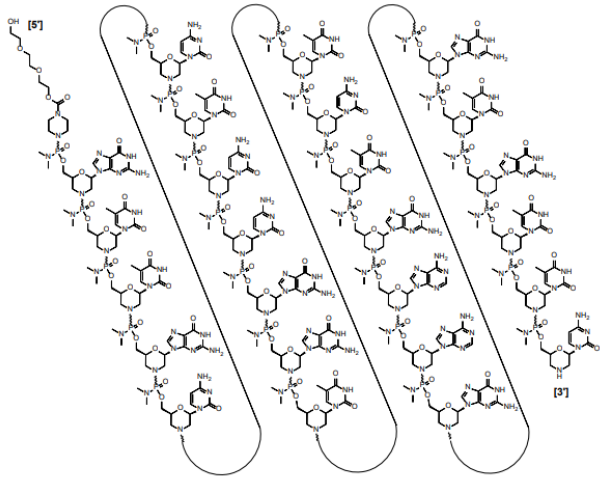
Claim #	Lim #	Limitation	Evidence
1	a	A solid-phase method of making	Sarepta (or any other manufacturer of VYONDYS 53 (golodirsen)) practices a solid-phase method of making an oligomer by manufacturing VYONDYS 53 (golodirsen): "The manufacture of the golodirsen drug substance is carried out in two processes that each consists of several sub-processes (stages) as outlined in Table 1. The first process is the drug substance synthesis process and it involves two stages: the ***solid-phase oligomer synthesis (SPOS)*** to produce the Oligomer-on-Resin as the final intermediate and the conversion of the final intermediate into the crude drug substance." SRPT-VYDS-0007054 (emphasis added).
1	b	an oligomer comprising	VYONDYS 53 (golodirsen) injection contains golodirsen, which is an oligomer: "Golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino **oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	c	a phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

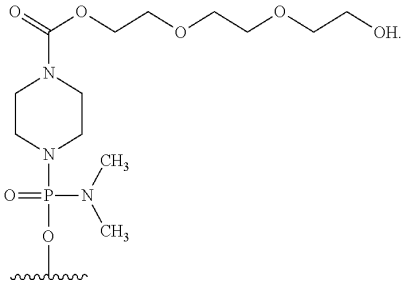
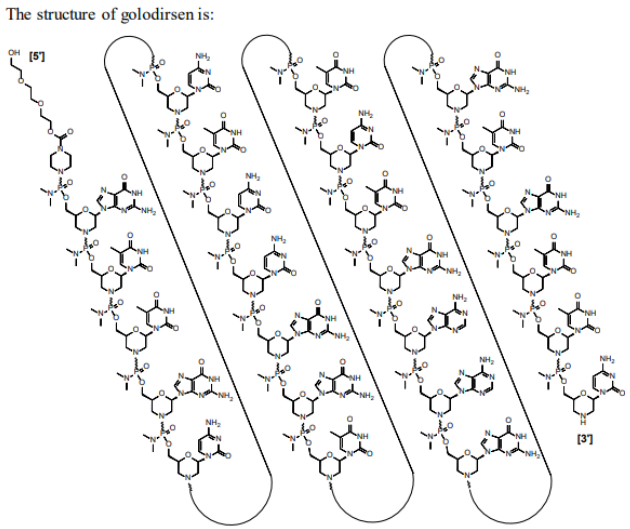
Claim #	Lim #	Limitation	Evidence
1	d	and a group at the 5′ end of said PMO,	VYONDYS 53 (golodirsen) injection contains golodirsen, which has a group at the 5′ end of the PMO: "The sequence of bases from the 5′ end to 3′ end [of golodirsen] is GTTGCCTCCGGTTCTGAAGGTGTTC." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. "The structure of golodirsen is:  " *Id.*
1	e	wherein said PMO is 100% complementary to the 36th to the 60th nucleotides from the 5′ end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5′ end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC.

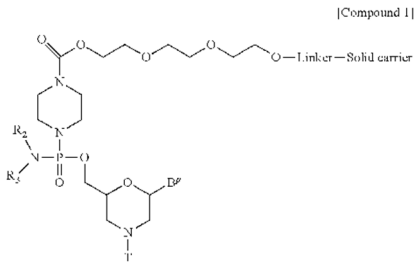
Claim #	Lim #	Limitation	Evidence
			'361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
1	f	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
1	g	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing,	VYONDYS 53 (golodirsen) hybridizes (or binds) to human dystrophin pre-mRNA (e.g., the target sequence) with Watson-Crick base pairing under physiological conditions: "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1

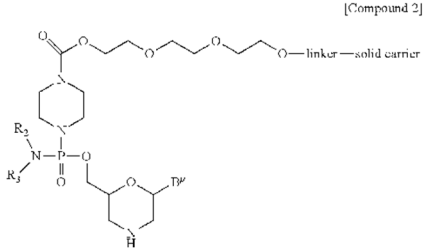
Claim #	Lim #	Limitation	Evidence
			[redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC.

Claim #	Lim #	Limitation	Evidence
			'361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53. Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4.

Claim #	Lim #	Limitation	Evidence
			[redacted]
1	h	wherein the phosphorodiamidate morpholino monomers of said PMO have the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen): The structure of golodirsen is:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	i	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine:

Claim #	Lim #	Limitation	Evidence
			"Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	j	wherein the group at the 5' end of said PMO has the formula:  .	The 5' end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
1	k	said method comprising:	[redacted]

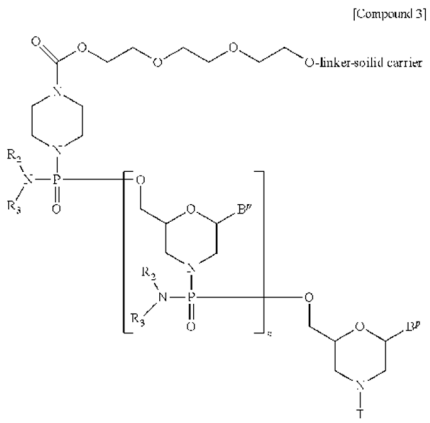
Claim #	Lim #	Limitation	Evidence
			[redacted]
1	l	a) providing Compound 1:  wherein T represents trityl, monomethoxytrityl, or dimethoxytrityl; wherein each of R2 and R3 represents a methyl; and wherein BP is a protected Base,	[redacted]

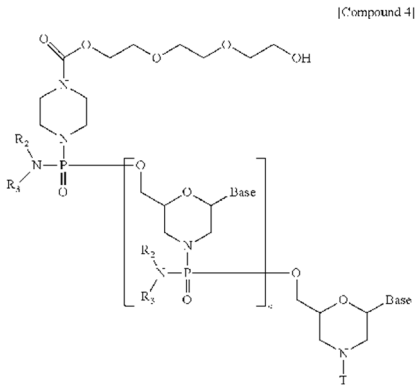
Claim #	Lim #	Limitation	Evidence
1	m	b) reacting said Compound 1 with an acid to form Compound 2: [Compound 2] 	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
1	n	c) reacting said Compound 2 with a morpholino monomer in the presence of a base and a solvent;	

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
1	o	d) repeating steps b) and c) until Compound 3 is complete:  	Nippon Shinyaku may rely upon any evidence cited for steps b) and c) to show each of those steps. Moreover [redacted]: [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
1	p	e) reacting said Compound 3 with a deprotecting agent to form Compound 4:  [Compound 4]	

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] First, on July 3, 2023, the Court issued its Memorandum Opinion (D.I. 248) and Order (D.I. 249) on claim construction. In relevant part, the Court ruled: • That step e) should be construed according to its "plain and ordinary meaning, which means 'chemically reacting Compound 3 with a deprotecting agent to form Compound 4" (D.I. 249 at 2); and • That step f) should be construed according to its "plain and ordinary meaning, which means 'chemically reacting Compound 4 with an acid to form the oligomer [or the PMO]" (D.I. 249 at 2). Importantly, the Court rejected Sarepta's attempt to limit each step to only direct reactions, stating "the claimed method does not exclude additional, unrecited reagents, ingredients, or other indirect reactions." D.I. 248 at 34.

Claim #	Lim #	Limitation	Evidence
			Further, the Court also rejected Sarepta's attempt to impose a step order, stating that "a person of ordinary skill in the art would understand that the order of steps e) and f) is not relevant to the claimed method" and including a parenthetical that "steps e) and f) are 'polishing' or 'finishing' steps and can be performed in any order because they are dependent on the purification methods available to a person of ordinary skill in the art." D.I. 248 at 37-38. Second, on July 11, 2023, Sarepta served its Non-Infringement Charts, identifying, for the first time a contention that the application of the doctrine of equivalents in this case "ensnares the prior art." *See, e.g.,* Sarepta Final Non-Infringement Contentions, Ex. A-7 at 17-19. As Sarepta acknowledges, it bears the "burden of producing evidence of prior art to challenge a hypothetical claim." *Id.* at 18 (citing *Interactive Pictures Corp. v. Infinite Pictures, Inc.*, 274 F.3d 1371, 1380-81 (Fed. Cir. 2001)). Sarepta had not identified this contention or any prior art that was allegedly ensnared by the application of the doctrine of equivalents to steps e) and f). [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
			Second, Sarepta has contended that the application of the doctrine of equivalents in this instance would ensnare the prior art. This is not the case. Under Federal Circuit, in order for the doctrine of equivalents to ensnare the prior art, the prior art must disclose ***all limitations*** of the claim (i.e., the claim as a whole), not just the limitation that is the subject of the doctrine of equivalents hypothetical. *See Abbott Laboratories v. Dey, L.P.*, 287 F.3d 1097, 1106, (Fed. Cir. 2002) ("The district court erred by comparing only the phospholipid limitation of claim 1 to the '301 patent (the only prior art considered by the court), while ignoring other limitations of the claim."); *Fiskars, Inc. v. Hunt Mfg. Co.*, 221 F.3d 1318 (Fed. Cir. 2000) ("A claim to a mechanical device usually recites a combination of several elements, most or all of which may be separately known. That an element of an accused device already existed does not bar equivalency as to that element."); RF

Claim #	Lim #	Limitation	Evidence
			Delaware, Inc. v. Pacific Keystone Technologies, Inc., 326 F.3d 1255, 1267, 66 U.S.P.Q.2d 1593 (Fed. Cir. 2003) ("Simply because a filter having a monomedia filter layer is in the prior art does not establish that the remaining limitations of the claimed invention are also in the prior art."). Here, the claim requires an oligomer "that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA." The prior art identified by Sarepta does not disclose or render obvious the specific oligomer that is required by the claim limitations. Therefore, the application of the doctrine of equivalents does not ensnare the prior art.
1	q	f) reacting Compound 4 with an acid to form said oligomer.	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] See also, element p above.
2	a	The method according to claim 1,	See claim 1.
2	b	wherein said acid used in step b) is trifluoroacetic acid.	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
3	a	The method according to claim 1,	See claim 1.
3	b	wherein said base used in step c) is N-ethylmorpholine	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

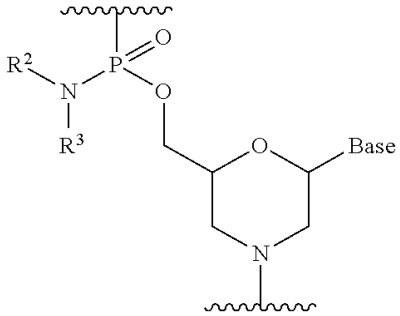
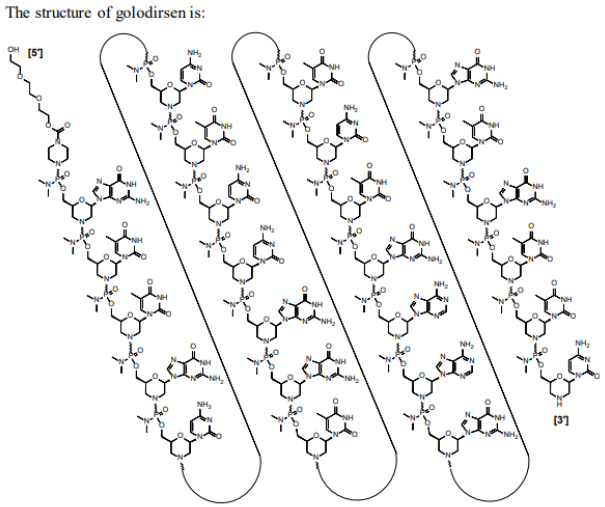
Claim #	Lim #	Limitation	Evidence
			Id. at 67.
3	c	and said solvent is N,N-dimethylimidazolidone.	[redacted]
4	a	The method according to claim 1,	See claim 1.
4	b	wherein said deprotecting agent is concentrated ammonia water used as a dilution with a solvent or a mixture of solvents.	[redacted]
5	a	The method according to claim 1,	See claim 1.

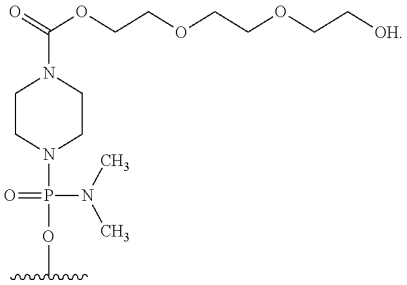
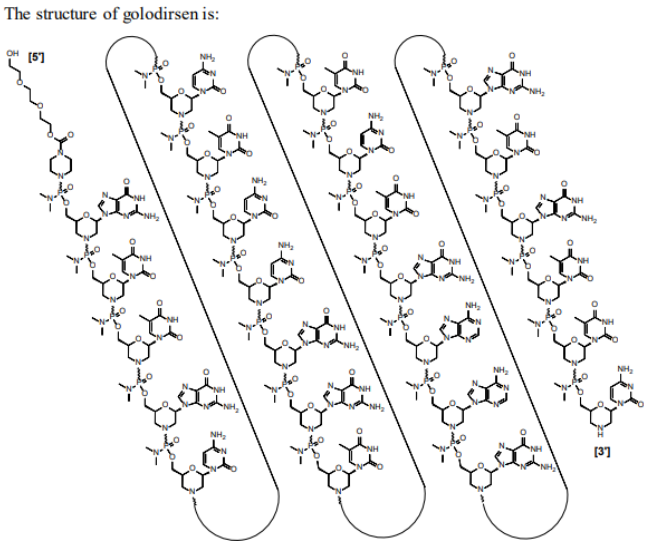
Claim #	Lim #	Limitation	Evidence
5	b	wherein said acid used in step f) is selected from phosphoric acid and hydrochloric acid.	[redacted]
6	a	A solid-phase method of making	
6	b	a phosphorodiamidate morpholino oligomer (PMO)	VYONDYS 53 (golodirsen) injection contains golodirsen, which is a phosphorodiamidate morpholino oligomer (PMO): "Golodirsen is an antisense oligonucleotide of the **phosphorodiamidate morpholino oligomer (PMO)** subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11 (emphasis added); *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

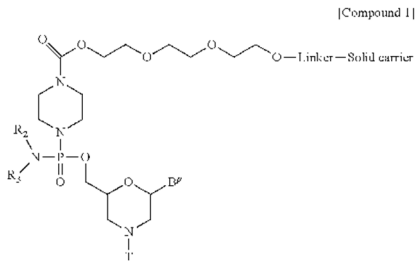
Claim #	Lim #	Limitation	Evidence
6	c	that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA,	The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). VYONDYS 53 (golodirsen) contains golodirsen, which is an oligomer of the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11. As shown above by comparing the two sequences, golodirsen is 100% complimentary to the 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA.
6	d	wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1,	This limitation is definitional of human dystrophin pre-mRNA, and is not specifically related to VYONDYS 53 (golodirsen). *See* '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent.
6	e	wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing,	[redacted]

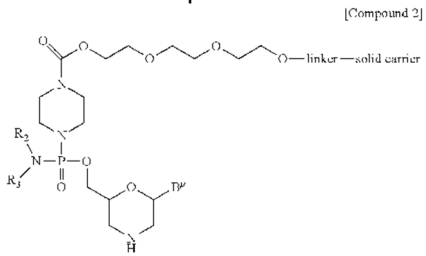
Claim #	Lim #	Limitation	Evidence
			"Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA . . . ." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 12.1 [redacted] Golodirsen contains the following nucleotide sequence from the 5' end to the 3' end: GTTGCCTCCGGTTCTGAAGGTGTTC. Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
			The 36th to 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA (e.g., the target sequence) are: GAACACCUUCAGAACCGGAGGCAAC. '361 Patent at Col. 47, SEQ ID 1; '361 Patent at Col. 6:38-39 ("The nucleotide sequence of exon 53 in the human wild type dystrophin gene is represented by SEQ ID NO: 1."); *see also* Equivalent disclosures from the remaining NS Asserted Patents as shown above for the '361 Patent; *https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* (explaining that in RNA, thymine (T) is replaced by Uracil (U)). In Watson-Crick base pairing, A (adenine) forms a base pair with T (thymine) or U (uracil), and G (guanine) forms a base pair with C (cytosine). *See https://link.springer.com/referenceworkentry/10.1007/978-3-642-11274-4_1683* Comparing the two sequences: Golodirsen: 5' – GTTGCCTCCGGTTCTGAAGGTGTTC – 3' Pre-mRNA: 3' – CAACGGAGGCCAAGACTTCCACAAG – 5' This comparison shows that golodirsen binds with the pre-mRNA (or target sequence) using Watson-Crick base pairing. Moreover, this binding occurs under physiological conditions, as it occurs inside a patient's body after being administered intravenously: **2.4 Administration Instructions** Application of a topical anesthetic cream to the infusion site prior to administration of VYONDYS 53 may be considered. VYONDYS 53 is administered via intravenous infusion. Flush the intravenous access line with 0.9% Sodium Chloride Injection, USP, prior to and after infusion. Infuse the diluted VYONDYS 53 over 35 to 60 minutes. Do not mix other medications with VYONDYS 53 or infuse other medications concomitantly via the same intravenous access line with VYONDYS 53.

Claim #	Lim #	Limitation	Evidence
			Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 2.4. [redacted]
6	f	wherein the phosphorodiamidate morpholino monomers of said PMO have the formula:  wherein each of R2 and R3 represents a methyl; and	Each of the 25 morpholino monomers of VYONDYS 53 (golodirsen) includes the claimed formula, as shown by the structure of VYONDYS 53 (golodirsen):  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.

Claim #	Lim #	Limitation	Evidence
6	g	wherein Base is a nucleobase selected from the group consisting of: uracil, cytosine, thymine, adenine, and guanine; and	Each Base in VYONDYS 53 (golodirsen) is either adenine, cytosine, guanine, or thymine: "Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine)." Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
6	h	wherein the 5' end of said PMO has the formula:  .	The 5' end of the PMO in VYONDYS 53 (golodirsen) matches the formula identified in the claim, as shown in the structure below:  Highlights of Prescribing Information (Dec. 12, 2019) § 11; *see also* SRPT-VYDS-0006978 - Highlights of Prescribing Information (Feb. 2021) § 11.
6	i	said method comprising:	[redacted]

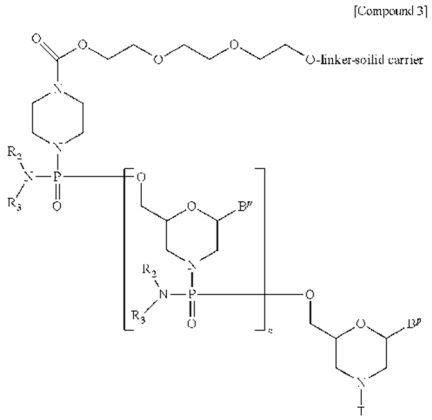
Claim #	Lim #	Limitation	Evidence
			[redacted]
6	j	a) providing Compound 1:  wherein T represents trityl, monomethoxytrityl, or dimethoxytrityl; wherein each of R2 and R3 represents a methyl; and wherein BP is a protected Base,	

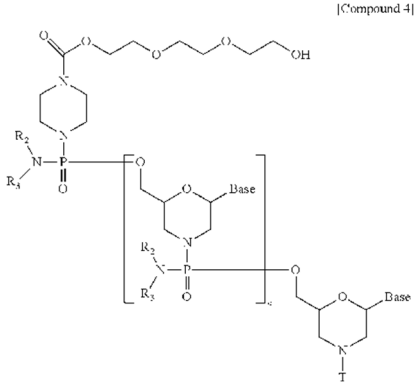
Claim #	Lim #	Limitation	Evidence
6	k	b) reacting said Compound 1 with an acid to form Compound 2: [Compound 2] 	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
6	l	c) reacting said Compound 2 with a morpholino monomer in the presence of a base and a solvent;	

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
6	m	d) repeating steps b) and c) until Compound 3 is complete: [Compound 3]  	Nippon Shinyaku may rely upon any evidence cited for steps b) and c) to show each of those steps.

Claim #	Lim #	Limitation	Evidence
			[redacted]
6	n	e) reacting said Compound 3 with a deprotecting agent to form Compound 4: [Compound 4] 	

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] First, on July 3, 2023, the Court issued its Memorandum Opinion (D.I. 248) and Order (D.I. 249) on claim construction. In relevant part, the Court ruled: • That step e) should be construed according to its "plain and ordinary meaning, which means 'chemically reacting Compound 3 with a deprotecting agent to form Compound 4" (D.I. 249 at 2); and • That step f) should be construed according to its "plain and ordinary meaning, which means 'chemically reacting Compound 4 with an acid to form the oligomer [or the PMO]" (D.I. 249 at 2). Importantly, the Court rejected Sarepta's attempt to limit each step to only direct reactions, stating "the claimed method does not exclude additional, unrecited reagents, ingredients, or other indirect reactions." D.I. 248 at 34.

Claim #	Lim #	Limitation	Evidence
			Further, the Court also rejected Sarepta's attempt to impose a step order, stating that "a person of ordinary skill in the art would understand that the order of steps e) and f) is not relevant to the claimed method" and including a parenthetical that "steps e) and f) are 'polishing' or 'finishing' steps and can be performed in any order because they are dependent on the purification methods available to a person of ordinary skill in the art." D.I. 248 at 37-38. Second, on July 11, 2023, Sarepta served its Non-Infringement Charts, identifying, for the first time a contention that the application of the doctrine of equivalents in this case "ensnares the prior art." *See, e.g.,* Sarepta Final Non-Infringement Contentions, Ex. A-7 at 17-19. As Sarepta acknowledges, it bears the "burden of producing evidence of prior art to challenge a hypothetical claim." *Id.* at 18 (citing *Interactive Pictures Corp. v. Infinite Pictures, Inc.*, 274 F.3d 1371, 1380-81 (Fed. Cir. 2001)). Sarepta had not identified this contention or any prior art that was allegedly ensnared by the application of the doctrine of equivalents to steps e) and f). [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

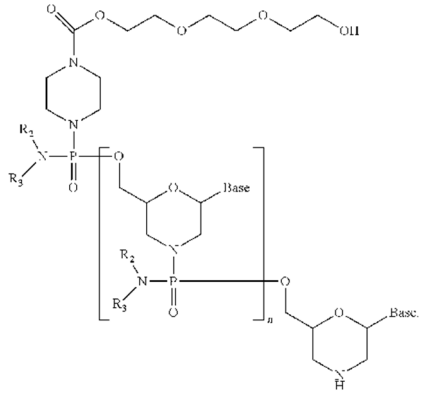
Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] NS further intends to rely on testimony and analysis provided by its expert witnesses, including Dr. Nathan Luedtke, to explain why Sarepta's process is insubstantially different and infringes under the doctrine of equivalents. Second, Sarepta has contended that the application of the doctrine of equivalents in this instance would ensnare the prior art. This is not the case. Under Federal Circuit, in order for the doctrine of equivalents to ensnare the prior art, the prior art must disclose ***all limitations*** of the claim (i.e., the claim as a whole), not just the limitation that is the subject of the doctrine of equivalents hypothetical. *See Abbott Laboratories v. Dey, L.P.*, 287 F.3d 1097, 1106, (Fed. Cir. 2002) ("The district court erred by comparing only the phospholipid limitation of claim 1 to the '301 patent (the only prior art considered by the court), while ignoring other limitations of the claim."); *Fiskars, Inc. v. Hunt Mfg. Co.*, 221 F.3d 1318 (Fed. Cir. 2000) ("A claim to a mechanical device usually recites a combination of several elements, most or all of which may be separately known. That an element of an accused device already existed does not bar equivalency as to that element."); RF

Claim #	Lim #	Limitation	Evidence
			Delaware, Inc. v. Pacific Keystone Technologies, Inc., 326 F.3d 1255, 1267, 66 U.S.P.Q.2d 1593 (Fed. Cir. 2003) ("Simply because a filter having a monomedia filter layer is in the prior art does not establish that the remaining limitations of the claimed invention are also in the prior art."). Here, the claim requires an oligomer "that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA." The prior art identified by Sarepta does not disclose or render obvious the specific oligomer that is required by the claim limitations. Therefore, the application of the doctrine of equivalents does not ensnare the prior art.
6	o	f) reacting said Compound 4 with an acid to form said PMO: 	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			First, on July 3, 2023, the Court issued its Memorandum Opinion (D.I. 248) and Order (D.I. 249) on claim construction. In relevant part, the Court ruled: • That step e) should be construed according to its "plain and ordinary meaning, which means 'chemically reacting Compound 3 with a deprotecting agent to form Compound 4" (D.I. 249 at 2); and • That step f) should be construed according to its "plain and ordinary meaning, which means 'chemically reacting Compound 4 with an acid to form the oligomer [or the PMO]" (D.I. 249 at 2). Importantly, the Court rejected Sarepta's attempt to limit each step to only direct reactions, stating "the claimed method does not exclude additional, unrecited reagents, ingredients, or other indirect reactions." D.I. 248 at 34. Further, the Court also rejected Sarepta's attempt to impose a step order, stating that "a person of ordinary skill in the art would understand that the order of steps e) and f) is not relevant to the claimed method" and including a parenthetical that "steps e) and f) are 'polishing' or 'finishing' steps and can be performed in any order because they are dependent on the purification methods available to a person of ordinary skill in the art." D.I. 248 at 37-38. Second, on July 11, 2023, Sarepta served its Non-Infringement Charts, identifying, for the first time a contention that the application of the doctrine of equivalents in this case "ensnares the prior art." *See, e.g.,* Sarepta Final Non-Infringement Contentions, Ex. A-7 at 17-19. As Sarepta acknowledges, it bears the "burden of producing evidence of prior art to challenge a hypothetical claim." *Id.* at 18 (citing *Interactive Pictures Corp. v. Infinite Pictures, Inc.*, 274 F.3d 1371, 1380-81 (Fed. Cir. 2001)). Sarepta had not identified this contention or any prior art that was allegedly ensnared by the application of the doctrine of equivalents to steps e) and f). [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] Second, Sarepta has contended that the application of the doctrine of equivalents in this instance would ensnare the prior art. This is not the case. Under Federal Circuit, in order for the doctrine of equivalents to ensnare the prior art, the prior art must disclose ***all limitations*** of the claim (i.e., the claim as a whole), not just the limitation that is the subject of the doctrine of equivalents hypothetical. *See Abbott Laboratories v. Dey, L.P.*, 287 F.3d 1097, 1106, (Fed. Cir. 2002) ("The district court erred by comparing only the phospholipid limitation of claim 1 to the '301 patent (the only prior art considered by the court), while ignoring other limitations of the claim."); *Fiskars, Inc. v. Hunt Mfg. Co.*, 221 F.3d 1318 (Fed. Cir. 2000) ("A claim to a mechanical device usually recites a combination of several elements, most or all of which may be separately known. That an element of an accused device already existed does not bar equivalency as to that element."); RF *Delaware, Inc. v. Pacific Keystone Technologies, Inc.*, 326 F.3d 1255, 1267, 66 U.S.P.Q.2d 1593 (Fed. Cir. 2003) ("Simply because a filter having a monomedia filter layer is in the prior art does not establish that the remaining limitations of the claimed invention are also in the prior art."). [redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted] .
7	a	The method according to claim 6,	See claim 6.
7	b	wherein said acid used in step b) is trifluoroacetic acid.	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
8	a	The method according to claim 6,	See claim 6.
8	b	wherein said base used in step c) is N-ethylmorpholine	[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]

Claim #	Lim #	Limitation	Evidence
			[redacted]
8	c	and said solvent is N,N-dimethylimidazolidone.	

Claim #	Lim #	Limitation	Evidence
			[redacted]
9	a	The method according to claim 6,	See claim 6.
9	b	wherein said deprotecting agent is concentrated ammonia water used as a dilution with a solvent or a mixture of solvents.	[redacted]
10	a	The method according to claim 6,	See Claim 6.
10	b	wherein said acid used in step f) is selected from phosphoric acid and hydrochloric acid.	[redacted]